TRANSACTIONS

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of
OPHTHALMOLOGY
and
OTOLARYNGOLOGY

MAY - JUNE
1951

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1. Taft, L.: Clinical Allergy, Philadelphia, W. B. Saunders Co., 1947, pp. 333-336.
2. Hinsie, F. G.: Allergy of the Nose and Paranasal Sinuses, St. Louis, C. V. Mosby Co., 1936, p. 269.
3. Zeller, S. F.: Causes of Sympathomimetic Amines, Cornell Conference on Therapy, D. 1947, p. 154.

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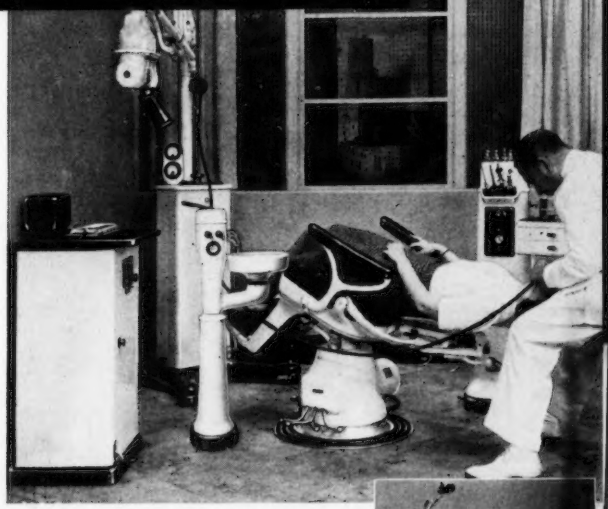

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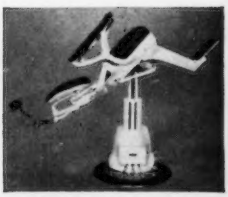

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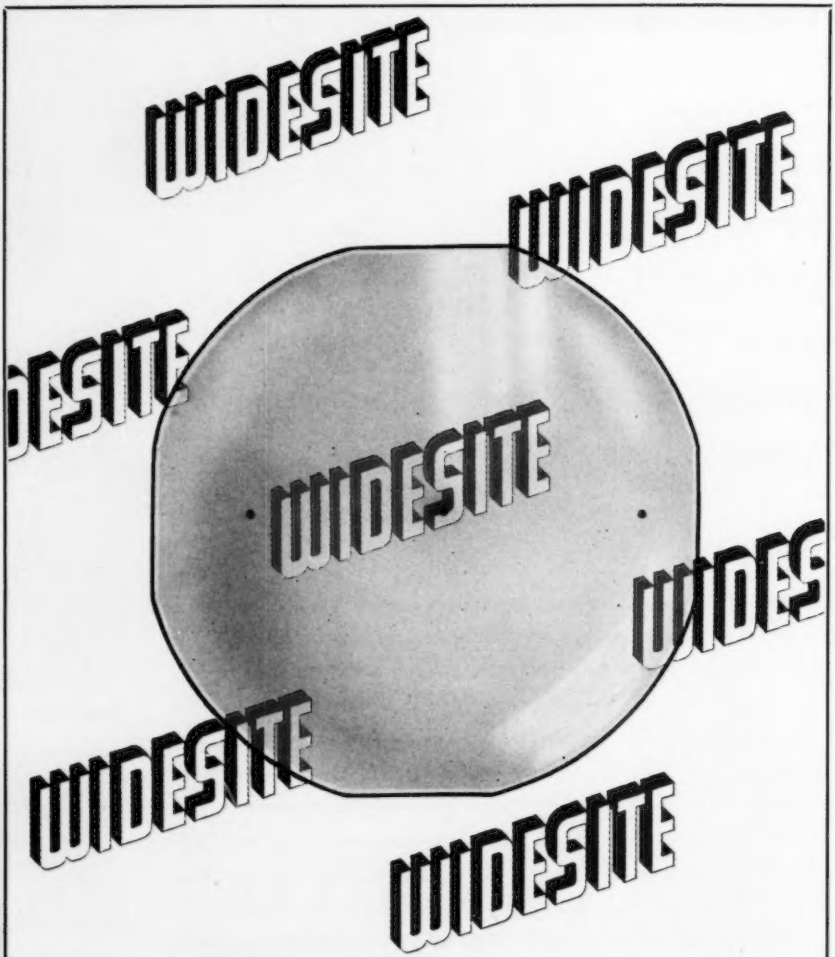

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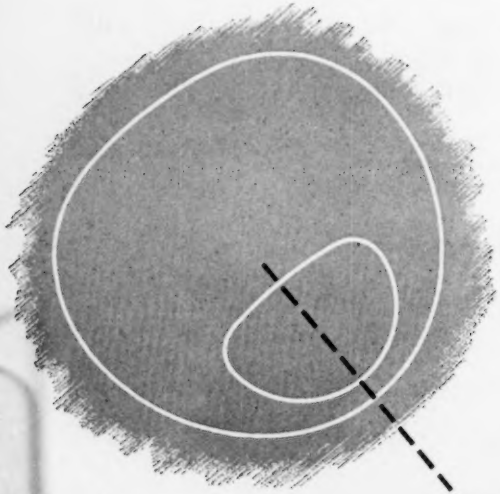

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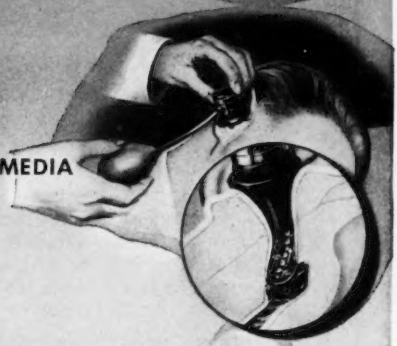

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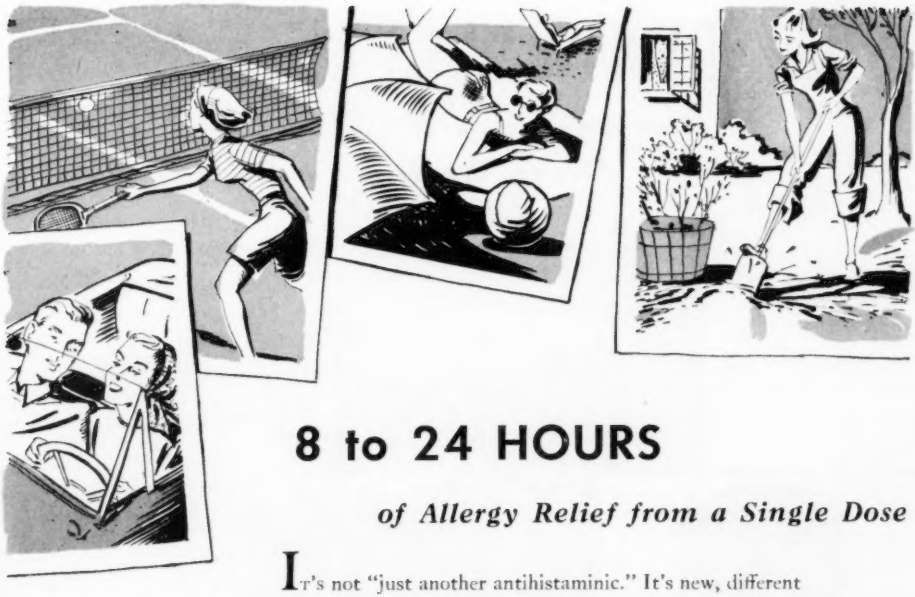

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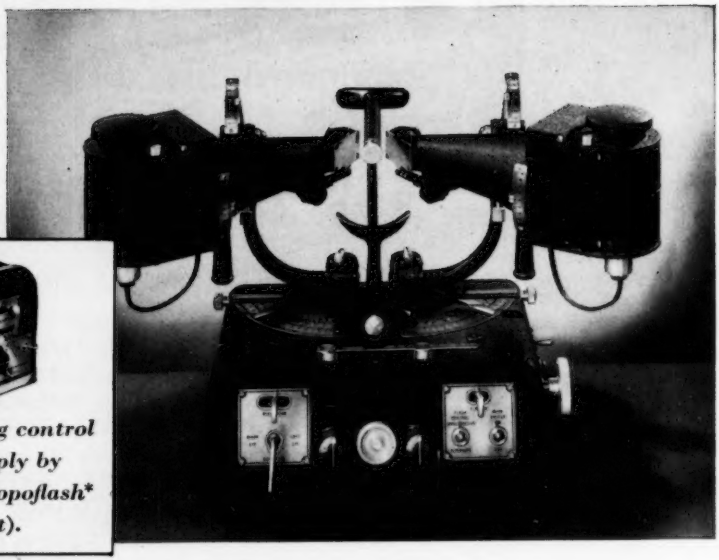

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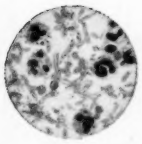

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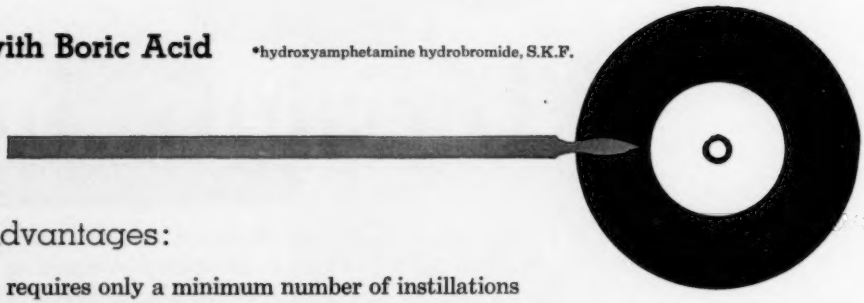

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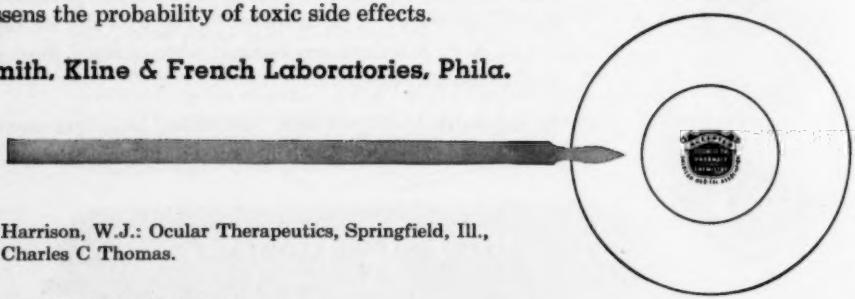

1. Harrison, W.J.: Ocular Therapeutics, Springfield, Ill., Charles C Thomas.

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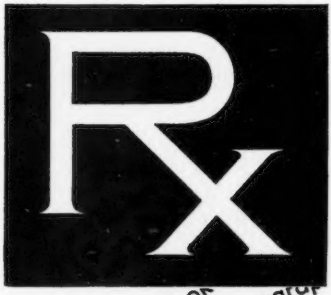

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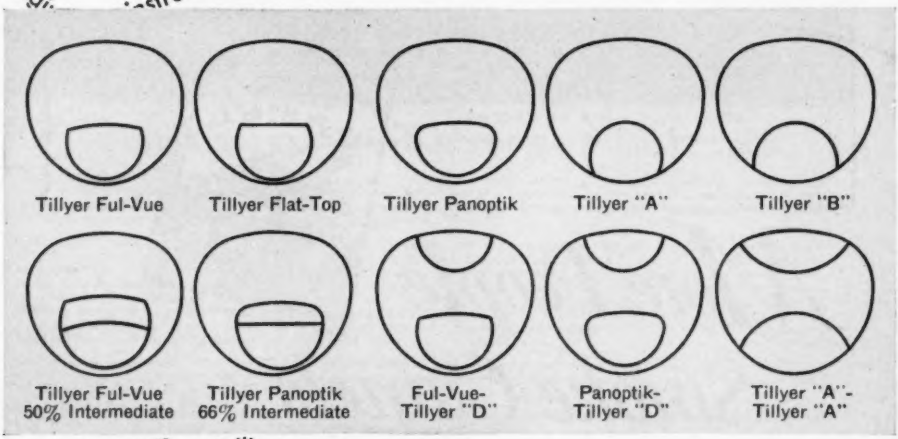

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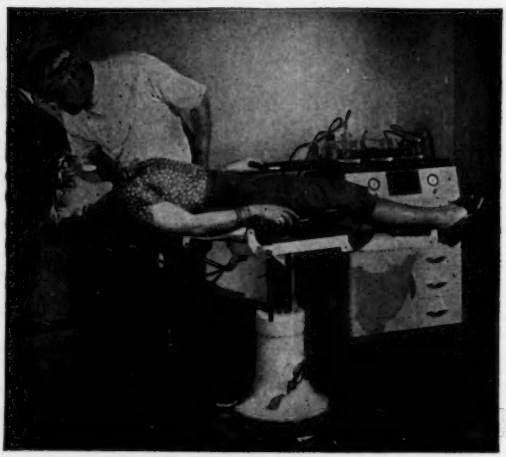

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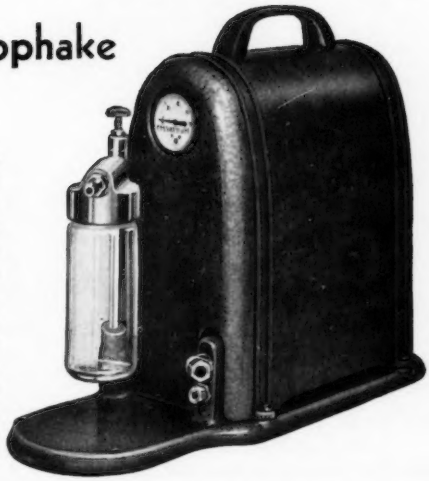

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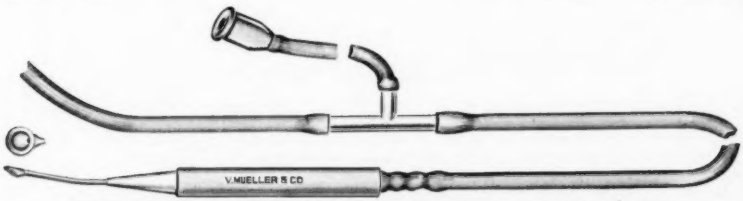

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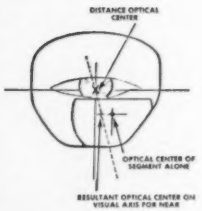

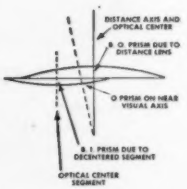
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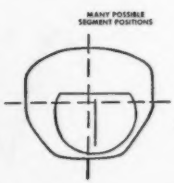

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COLLAGEN DISEASES: THEIR RELATION TO EFFECTS OF ADRENAL CORTICAL AND PITUITARY ADRENOCORTICOTROPIC HORMONES

HOWARD F. POLLEY, M.D.
ROCHESTER, MINN.
BY INVITATION

THE term "collagen diseases" is used to designate a group of diseases of unknown etiology affecting multiple systems of the body and formerly considered to be unrelated because of their widely varying (though sometimes overlapping) clinical manifestations.

DISEASES INCLUDED

Diseases usually included in this category are periarteritis nodosa, rheumatic fever, rheumatoid arthritis, lupus erythematosus, scleroderma, dermatomyositis and serum sickness. Glomerulonephritis and malignant hypertension also belong to this list, according to Aegerter and Long.[1] In collecting this group your colleagues in internal medicine and pathology have (unintentionally, no doubt) omitted certain inflammatory ocular diseases which probably should be included. Since these are to be discussed later in this meeting, I shall not list them. Even more alteration of the list may be needed if a favorable response of various diseases to adrenal and pituitary hormones is to become one of the criteria for inclusion in the group of collagen diseases. At present, understanding of collagen or mesenchymal diseases is so incomplete that only tentative conclusions are warranted.

DERIVATIVES OF MESENCHYME

Mesenchymal derivatives are diffusely located throughout the body and, in addition to the connective tissue and fibroblasts, consist of cartilage (chondroblast), bone (osteoblast), muscle and the reticulum or reticulo-endothelial component of lymph nodes, spleen, liver and bone marrow. There are both circulating and fixed tissue components. Immune globulin (circulating antibody) and collagen are products of the reticulum and are related chemically to hyalin, the homogeneous matrix produced by cartilage, and to osteoid tissue, the product of the osteoblast. It is known that chondroitinsulfuric acid, the chief organic chemical constituent of cartilage, is closely related chemically to mucoitinsulfuric acid, which is the chief organic chemical constituent of both the vitreous humor and the synovial fluid.

PATHOLOGY

The recognized pathologic changes common to collagen diseases consist of swelling of the mucoid ground substance of connective tissue, proliferation of fibroblasts and derivatives of reticulum and cellular infiltration of the tissues, which may be followed by degenerative and later by tissue reactions of necrosis. Fibrinoid degeneration of the collagen of capillary walls and the media of arterioles, with increased permeability resulting therefrom, is said to be the earliest organic change observed in these diseases. Thus the vascular component of collagen diseases is an important and, in certain instances, the predominant manifestation of diseases of this group.

PATHOGENESIS

This group of diseases is generally thought to be due to a hypersensitivity

From the Division of Medicine, Mayo Clinic.
Presented at the Fifty-Fifth Annual Session of the American Academy of Ophthalmology and Otolaryngology, Oct. 8-13, 1950, Chicago, Ill.

type of reaction which usually lacks the abruptness of onset and severity of effects characteristic of anaphylaxis. Stated briefly, the reaction of hypersensitivity is an abnormal activity of both the circulating and fixed tissue components of the mesenchyme, which functions as the defense organ. Alteration of the antigen-antibody reaction is thereby produced but the nature of the allergen or allergens causing collagen diseases is still obscure.[10] It is more appropriate, therefore, to regard such diseases as affected by infection rather than caused by infection. Altered endogenous proteins produced by chemicals, such as iodine and sulfonamides, or by undue exposure to such physical agents as cold, heat, and sunlight have been demonstrated both experimentally[10] and clinically, especially in such diseases as periarteritis nodosa and lupus erythematosus.

The entire system of mesenchymal derivatives may be regarded as a unit or organ of defense[1] involving both protective or immune reactions and reparative functions. When stimulation of the immune reaction or reparative processes is excessive or abnormal, the reactions of fibrinoid degeneration, proliferation and other characteristics of the tissue responses in this group of diseases may be produced and disease states result.

RELATIONSHIP BETWEEN COLLAGEN DISEASES AND FUNCTION OF THE ADRENAL CORTEX

It is pertinent at this time to consider the basis for a relationship between the physiologic and pathologic phenomena of the collagen diseases and the adrenal hormones. As has already been outlined, diseases of collagen have long been thought related to immune processes. Quite independently, the relation of the adrenal glands to immune reactions has been extensively investigated.[3] That there is an inverse relationship between the activity of the adrenal cortex and the amount of lymphoid tissue is fairly definitely established. A further relationship is readily recognized in the long-known fact that the adrenal cortex is essential for proper maintenance of the organism in extremes of heat and cold, infections and trauma.[1] The action of adrenal hormones is undoubtedly widespread on tissues of mesenchymal origin.[14]

Among the physiologic processes known to be affected by hormones of the adrenal cortex are (1) control of permeability and transfer of inorganic ions and water between extracellular and intracellular tissues (and from blood to urine), and (2) activation of enzymes. Studies of adrenal insufficiency indicate that the profound alterations of function of many organs can be controlled to a large measure by regulation of intake of inorganic ions and that multiple enzyme systems are usually affected.[11]

The close relationships of inorganic ions, activation of enzymes and adrenal cortical hormones is well exemplified in the deposition of glycogen in the liver. In such an action the potassium (K) ion has an important, if not dominating, effect.[11]

Hyaluronidase is one of the enzymes being widely studied in connection with the collagen diseases. The presence of a disturbed equilibrium between hyaluronic acid and hyaluronidase in connective tissue diseases has been repeatedly demonstrated.[10] The hyaluronidase-inhibiting activity of the serum, however, may be a nonspecific feature of the defense reaction which operates in varying degree with the degree of the individual's susceptibility.[5]

Either by mechanisms already mentioned or others yet to be recognized, steroid hormones alter the tissue reaction that follows union of antigen and antibody. By such action the harmful

effects of hypersensitivity may be dissociated from the beneficial reactions of immunity.[16] Whether this effect occurs at the level of antibody production, at the level of union of antigen and antibody or at any other point in the development of the immune response is not definitely established.[3]

The widespread effects of adrenal function on mesenchymal and lymphoid tissue, as well as certain metabolic effects, are produced only by those steroid hormones which have an oxygen atom at the carbon atom position number 11. Such preparations are thus sometimes referred to as C-11 oxygenated steroids.[14]

Of the C-11 oxygenated steroids, cortisone appears to be one of the most, if not the most, potent.[13] The fate of this substance after injection is still unknown. Present evidence suggests that it is either directly utilized or converted to a closely related, more utilizable form. In this connection it is interesting to note that while pituitary adrenocorticotropic hormone produces effects similar, if not identical, to those of cortisone, experimental[6] and clinical laboratory evidence[12] suggest that not cortisone but another C-11 steroid with antirheumatic activity, compound F, is the product of the responsive adrenal gland stimulated by pituitary adrenocorticotropic hormone.

EFFECTS OF CORTISONE AND PITUITARY ADRENOCORTICOTROPIC HORMONE

It took thirteen years each for cortisone and pituitary adrenocorticotropic hormone to be separated, identified and prepared for clinical investigation. Pioneer investigators hoped the two hormones would be found useful in managing diseases of pituitary and adrenal glands and perhaps other endocrine diseases. In time these modest hopes have been fulfilled.[7]

As you now know, cortisone and pituitary adrenocorticotropic hormone not only influence relatively rare endocrine conditions but have a prompt and profound effect on fibrous tissue, muscle, lymphoid tissue and the so-called hyperergic state—the tissues and the reaction characterizing the collagen or mesenchymal diseases. Cortisone and pituitary adrenocorticotropic hormone are both antirheumatic and anti-allergic. They act at the tissue level—especially important and desirable to the ophthalmologist and otolaryngologist — but do not kill germs, nor do they "cure" diseases the symptoms of which they may suppress.[9] But in some manner, perhaps simply by supplying extra adrenal hormone,[14] they provide susceptible tissues with a shield against a wide variety of irritants.

Considered conservatively, there are ten to twelve nonhormonal diseases presumed to have widely differing etiology which can be markedly modified or temporarily suppressed by either cortisone or pituitary adrenocorticotropic hormone. This is all the more remarkable because most of these diseases, heretofore, have been peculiarly resistant to control or even temporary modification.[7]

We can be optimistic regarding the therapeutic usefulness of these hormones, but their judicious use will be more assured if two principal limitations are fully appreciated: (1) Effects are usually, though not always, transient. (2) Hormones are capable of adverse as well as beneficial effects.[7]

Clinical Effects of Cortisone and Pituitary Adrenocorticotropic Hormone on Rheumatoid Arthritis

The beneficial effects of cortisone and pituitary adrenocorticotropic hormone can be summarized by relating briefly the reactions noted in patients with reversible rheumatoid arthritis. In almost every suitable case of rheumatoid

arthritis, within a few days—often indeed within a few hours—complete or nearly complete reversal begins.

The fibrous tissue seems to be affected first as indicated by the marked reduction of stiffness. Articular pain, swelling and tenderness are reduced and deformities are often corrected. Maximal subjective improvement usually occurs within eight days, objective improvement within two to three weeks, but progress continues thereafter, perhaps for several months. The antirheumatic effects were very marked in 13 of our first series of patients with rheumatoid arthritis, marked in 9, and moderate in 1.[8]

Strength, appetite and weight are increased. A ravenous appetite is experienced by some patients, but weight tends to stabilize after lost weight is regained. Euphoria may occur with increased mental and physical energy. Fever, rheumatoid nodules and enlarged lymph nodes disappear or subside. Of 31 flexion contractures, two thirds or more disappeared in three to twenty-one days; the remainder were markedly improved. Biopsy of synovial membrane revealed marked reduction of the inflammatory reaction following administration of either cortisone or pituitary adrenocorticotropic hormone.[8]

Responses to repeated courses are essentially similar. Usual doses of cortisone have been 100 mg. daily, sometimes 200 or 300 mg. on the first days of treatment; usual doses of pituitary adrenocorticotropic hormone have been 40 to 100 mg. in divided doses three to four times daily. When administration of the hormones was discontinued, prompt relapse occurred in about three fourths of our cases but in 20 to 25 per cent partial relapse, delayed relapse or fairly prolonged remission occurred.

DISEASE VERSUS RESIDUES OF DISEASE

In any disease one must distinguish sharply between two distinct features, the tissue reactions (physiologic processes) which constitute the disease per se and the residues of the disease (anatomic changes).

These hormones influence chiefly the inflammatory reactions of the active disease, not the residues of the disease. To use a figure of speech, they act as a fire shield but do not per se put out the fire nor act as carpenters to repair fire's damage.[9] Therefore, results will differ greatly depending on the stage of the disease present at the time the hormone is administered.

If the hormone is given early and little or no significant residues are present, temporary results may be more or less complete. If only small amounts of active inflammation are superimposed on much old destructive change, the results may be quite limited. These principles operate in inflammatory ocular diseases as well as in inflammatory articular diseases.

HYPERCORTISONISM

Cortisone and pituitary adrenocorticotropic hormone are potent agents capable of influencing many tissues of the body. They have physiologic effects other than those which are antirheumatic and anti-allergic. These are signs of hyperadrenalism designated "cortisone-hyperadrenalism" or "hypercortisonism" to differentiate them from other causes of hyperfunction of the adrenal cortices.

In 74 per cent of our first series of cases of rheumatoid arthritis, adrenal dysfunction was clinically not apparent or very mild. Moderate to marked evidence of hypercortisonism occurred in 26 per cent.[8]

Doses of cortisone or pituitary adrenocorticotropic hormone required to suppress inflammation in affected tissues are relatively high when compared to the amount needed to correct deficiency due to total glandular insufficiency. These relatively high doses are sometimes well tolerated, sometimes not. Individual tol-

erance varies but most signs of hypercortisonism are produced by repeated daily doses of 200 mg. of cortisone or physiologically equivalent amounts of pituitary adrenocorticotropic hormone, or when daily doses of 100 mg. of cortisone or physiologically equivalent amounts of pituitary adrenocorticotropic hormone are given for a long period, usually more than four to seven weeks. This is especially true when the hormones are given to menopausal women and adolescents. The various reactions noted include acne, edema, cutaneous striae, mental changes of varying intensity, muscular weakness and rounding of the face. These and others are described and discussed in detail elsewhere.[8,15] No significant increases in blood pressure have occurred in our rheumatoid patients, but these hormones, especially pituitary adrenocorticotropic hormone, may increase blood pressure in patients with renal disease.

The biochemical changes occurring from large doses or prolonged administration of either cortisone or pituitary adrenocorticotropic hormone can be summarized briefly. The excretion of 17-ketosteroids in urine is increased markedly while pituitary adrenocorticotropic hormone is being administered and is decreased as a result of cortisone; this decrease may persist for weeks after use of the hormone is stopped. Excretion of corticosteroids is temporarily increased by both cortisone and pituitary adrenocorticotropic hormone.[15] Electrolyte imbalance when it does occur usually consists of a hypochloremic, hypopotassemic alkalosis and tends to develop when large doses of either cortisone or pituitary adrenocorticotropic hormone are employed or after prolonged administration of the usual daily doses. Temporary impairment of carbohydrate tolerance of clinical importance occurs only in susceptible persons. Decrease of the circulating eosinophils is considered evidence of adrenal cortical suppression and occurs with use of both cortisone and pituitary adrenocorticotropic hormone, though perhaps to a greater degree with the latter.

Hypercortisonism has been likened to "Cushing's syndrome." Practically all of the features of this syndrome have been collectively observed in our early experience.[8,15] Currently, by better dosage control none or only one or two features of hypercortisonism may be encountered in any individual case.

Irrespective of the degree or extent of the signs of hypercortisonism, reversibility begins rather rapidly when administration of the hormone is discontinued. Fewer side effects are developing as better methods of using these hormones are being developed.

CURRENT MANNER OF USAGE OF CORTISONE AND PITUITARY ADRENOCORTICOTROPIC HORMONE

Because of the nature of the potential side effects, these hormones should be used with caution in the presence of (1) hypertensive cardiovascular disease, including glomerulonephritis, cardiac decompensation and old rheumatic carditis with limited cardiac reserve, (2) diabetes mellitus, (3) active tuberculosis, (4) latent or frank psychoses[7] and (5) marked osteoporosis.[2]

In order to find the optimal methods of treatment with cortisone and pituitary adrenocorticotropic hormone, various methods of administration are being investigated. These include (1) repeated courses with the usual full dosage interrupted by rest periods, (2) initial full doses followed by smaller maintenance doses daily or less often, (3) alternated administration of cortisone and pituitary adrenocorticotropic hormone with repeated courses as in the first method, and (4) combined use of cortisone and pituitary adrenocorticotropic hormone either in repeated courses or as in the second method.[9]

In all instances the objective is the same: to attempt to cooperate with rather than to dominate or supplant the functions of the pituitary-adrenal mechanism. Thus, it is entirely possible that no single plan of treatment will be equally satisfactory for all diseases for which the hormones may be used or even for all patients with the same disease.

Investigative studies with cortisone given orally are also in progress. The early results are as good as those from intramuscular administration.[4,17] This development may lead to further revision of current concepts of administration of cortisone as well as of pituitary adrenocorticotropic hormone. Local applications of cortisone to the eye and to the ear, nose, and throat are also a promising development of especial interest to this group.

SUMMARY

The adrenal cortical hormone, cortisone, and pituitary adrenocorticotropic hormone have marked effects on the metabolism of fibrous, muscular and articular tissues and the other tissues affected in collagen or mesenchymal diseases.

The specific mode of action is not yet defined and there is much yet to be learned.

Physiologic reactions of overdosage or intolerance have been reversible.

Finally, it is anticipated that with increased availability of cortisone and pituitary adrenocorticotropic hormone, their optimal methods of use can soon be established.

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THE ANTIBIOTICS

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BY INVITATION

I HAVE been honored and very fortunate to have been invited to come out here for the past three years as an instructor. I have talked to a lot of you about the sulfonamides and the antibiotics. Now I will tell you the truth. This is the first time that I have ever talked about antibiotics when I really know what I am talking about. I will tell you why.

Mrs. Long and I were fortunate enough to be able to go to Europe for the months of May, June, and July. Starting in June, in Amsterdam, we ran into the most delicious strawberries I have ever eaten. But, being a professor of preventive medicine and very cautious, I said, "Now, none of that cream for me. I don't want to get anything. I don't know whether the milk is pasteurized." So I ate strawberries in Holland, in Denmark, in Sweden, and in Finland. Then, when we got to Norway, strawberries had gone out of season a bit, and were a little more expensive than they had been. So Mrs. Long, being a Yankee, stopped eating strawberries for breakfast and took something cheaper. But I, of course, being the expansive male in the family, said, "Well, they are not very expensive. I will have them." In Norway they had some especially delicious cream. I inquired about it and of course they said it was pasteurized, so I had strawberries and cream.

We got home the twenty-fourth of July, and four days later we were driving up to Martha's Vineyard. At about Aberdeen I thought I was coming down with Dr. Francis' favorite virus; in other words, influenza. I felt just like a patient suffering from it. To make a long story short, it took me and six other doctors who piled in on me, I might say literally, to look after me when they heard I was sick. One of them, who was one of my oldest and best friends, wanted to give me calomel. I did not dare refuse him and decided I would hold it in my hand and wait until he left. I thought the best way to get rid of it was to put it down the toilet immediately rather than have it go down a little later. After about three weeks, it became perfectly clear that I had acute undulant fever.

I thought to myself, "I have told a lot of people just how to treat this disease, and I have treated a lot of people who have had it. I am going to treat myself the way I treat my patients." Before I had taken aureomycin for a week it took all the courage that I possessed even to think of another dose of aureomycin. Now I can tell you a great deal about aureomycin, as you can well imagine. Well, to get down to the serious part of my purpose in being here—I am well. I took enough aureomycin, and I am sure I am all right. I don't even worry about it. (Dr. Long has had no relapses. Ed.)

Five years ago this time, if one were going to talk on antibiotics, it would have been a relatively simple thing because one would have said, "Use penicillin for conditions in which it is indicated," and that would have been that. Four years ago it had become a little more difficult because, between 1944 and 1946, Dr. Waksman and his colleagues and associates had developed strepto-

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mycin. But still it was not too hard, because one generally recommended the use of streptomycin in the gram-negative type of infections and the use of penicillin in the gram-positive infections. That happy situation lasted for a couple of years, until about 1948, when suddenly out of the blue, in less than two years, came three new powerful, widely effective, and easily usable antibiotics, the complete range of which is not quite certain at the present time. All three of them overlap each other in many respects in their clinical application. So today, any doctor who is faced with infection has to make up his mind which one of five antibiotics he is going to use, and then, if he uses one of the three newer antibiotics, he says, "Now, really, which one is going to be the best in this particular patient?"

Unfortunately, in the hospital today we are seeing so few untreated standard infections which can be used for testing antibiotics that I believe the day is almost past in this country when we can, with good controls, test the comparative therapeutic effects of new antibiotics. There are just not enough patients. Take our situation at Johns Hopkins. Back in 1938, when we first used sulfapyradine, it was not hard to get about two hundred cases of pneumococcal pneumonia in the winter. I doubt whether this winter we will have sixty cases in the hospital, and many of them will have been treated with something or other before they get to it. If one found an antibiotic this winter that one wanted to do comparative tests with, it would be difficult to make comparative tests in lobar pneumonia if one used all the hospital facilities in Baltimore. It would be hard to get enough patients because most patients are being treated at home.

As I pointed out last year, we closed our contagious hospital in Baltimore the thirty-first of December, 1949, because we did not have many patients. It is still true. We are seeing fewer and fewer patients, on the general medical wards, with infections. You may ask in a few minutes, when I begin to show you slides, "How are we going to make our choice? How are we going to arrive at the decision that one antibiotic is a little better than another?" One has to do three things now. First you have to study the *in vitro* bacteriostatic or bacterial effect. That is helpful. It does not give you the final answer though. Secondly, there are certain standard infections in mice, such as the hemolytic streptococcic peritonitis, which can be produced by using the strain C-203 that has been studied many years by many individuals. We know just what it will do in mice. Of course mice have practically no natural resistance to this infection, and we can use thousands of mice in our tests. We can vary the dosage of various antibiotics, and we can get a pretty good idea of their effectiveness against this type of infection. We can do the same thing with certain pneumococcic infections and with a type of Friedlander's bacillus infection. These infections give us very good information because, starting back fifteen years ago, we have found—and this is true of penicillin and streptomycin—that if an antibiotic or a sulfonamide is highly effective against these experimental diseases in mice, they will show about the same effectiveness against similar infections in human beings. Much of what I am going to talk about to you today is based on these two points:

In vitro in the mouse, and then as careful clinical observation and controls as one can get. But, as I have said, it is getting increasingly difficult to test clinically the new antibiotics.

I am going to report to you now the opinions of our department in Baltimore, which I think will agree pretty well with those of Dr. Harry Downing, Dr. Max Finland, and other groups of

TABLE I—CURRENT USAGE OF ANTIBIOTICS IN INFECTIONS

TYPE OF INFECTION	PENICILLIN	STREPTOMYCIN AND DIHYDROSTREPTOMYCIN	AUREOMYCIN	CHLORAMPHENICOL	TERRAMYCIN
Streptococcal Infections					
1. Beta Hemolytic	IA		IB	II	IB
2. Alpha Hemolytic	IA		IB	III	II
3. Non-Hemolytic	IA		IB	N	IB
4. All enterococci	II*	II*	IA	III	IB
Staphylococcal Infections	IB		IA		II
Pneumococcal Infections	IA		IB	II	IB
Neisserian Infections					
1. N. meningitidis	IA		N	N	N
2. N. gonorrhea	IA		II	II	II
Diphtheric Infections	Antitoxin + I		N	N	N
Tuberculous Infections		I + P.A.S.			
Anthrax Infections	IA		IA	N	N
Clostridial Infections					
1. Gas gangrene	I		N	N	N
2. Tetanus	?		N	N	N
Gram-Negative Bacillary Infections					
1. E. coli		II	IA	IB	IA
2. Kl. pneumoniae		II	IB	IA	IB
3. Proteus					
4. A. aerogenes		II	IB	IA	IA
5. Ps. aeruginosa		Polymyxin is best.			III
Salmonella Infections					
1. S. typhosa				I	
2. Others					
Shigella Infections			I	I	I
Pasteurella Infections					
1. P. pestis		I+S.D.	N	N	N
2. P. tularense			I	I	N
Brucella Infections					
1. Br. melitensis			IA	IB	IB
2. Br. suis			IA	IB	IB
3. Br. abortus			IA	IB	IB
Listerella Infections			I	N	N
Cholera			N	N	N
Hemophilis Infections					
1. H. influenza meningitis		II+S.D.	IB+S.D.	IA	
2. H. pertussis			N	N	N
3. H. ducreyi		II	I	I	I

N—Not evaluated
IA—First Choice
IB—Second Choice
II—Effective
III—Good
*—Use together
Blank—Not effective
P.A.S.—Paro-amino-salicylic acid
S.D.—Sulfadiazine

TABLE I—CURRENT USAGE OF ANTIBIOTICS IN INFECTION, Continued

TYPE OF INFECTION	PENICILLIN	STREPTOMYCIN AND DIHYDROSTREPTOMYCIN	AUREOMYCIN	CHLORAMPHENICOL	TERRAMYCIN
Spirochetal Infections					
1. T. pallidum	IA		II	II	II
2. T. pertenue	IA		N	N	N
3. T. carateum	IA		N	N	N
4. B. recurrentis	IA		N	N	N
5. B. vincenti	IA		N	N	N
6. L. icterohemorrhagica			I	N	N
D. granulomatosis		II	I	I	I
Bartonella Infections			N	I	N
Streptobacillary Infections		IA	N	IA	N
Bacteroidosis		II	IA	N	IA
Rickettsial Infections					
1. R. prowazeki			I	I	I
2. R. mooseri			I	I	I
3. D. rickettsi			IA	IA	IB
4. D. conori			I	I	I
5. R. akari			I	I	I
6. R. tsutsugamushi			IA	IA	IB
7. C. burneti			I	I	I
Viral Infections					
1. Psittacosis			I	I	N
2. L. venereum			I	I	N
3. Primary Atypical Pneumonia			IA	II	IB
4. Herpes Simplex					
5. Herpes Zoster			No General Agreement		
6. Chicken Pox			N	N	N
7. Vaccinia disseminata			I	N	N
8. Small Pox			N	N	N
9. Pleuro-pneumonia Infections			IA	IB	IA
10. Mumps or Measles					
11. Infectious Mononucleosis					
12. Epidemic Hepatitis					
13. Epidemic Kerato-Conjunctivitis					
14. Poliomyelitis					
15. Trachoma			I	N	I
16. The Common Cold and Influenza					
Parasitic Infections					
1. Acute Amebic Dysentery			I	I	I
Fungal Infections					
1. Actinomycosis	I+S.D.		N	N	N
Trichomonas vaginalis			I locally	N	N

N—Not evaluated
IA—First choice
IB—Second choice
II—Effective
S.D.—Sulfadiazine
Blank—Not effective

individuals, regarding the choice of the antibiotics today for the general systemic treatment of infections (table I).

In streptococcic infections, penicillin is the drug of choice, with the exception of enterococcic infection, where it seems generally agreed that aureomycin is the best. You will notice that I have put aureomycin as the drug of choice with staphylococcic infection, and that is based on the fact that Max Finland in Boston, Monroe Romansky in Washington, and other people, including ourselves, have found that the percentage of strains of staphylococci on primary isolation, before the treatment of patients, which are quite resistant to penicillin are increasing all the time.

What is apparently happening — not only in this country but also in England and Australia, and probably all over the world where much penicillin is being used—is that the non-penicillinase-producing strains of Staphylococcus aureus are being wiped out as the etiologic agents of disease. Whether they are killed off, or just what happens to them, one cannot say definitely. They are being replaced by staphylococci which produce penicillinase and hence are more or less resistant, depending upon how much penicillinase is produced, to the therapeutic effects of penicillin. Hence, we put aureomycin first.

In pneumococcic infection, use penicillin. In neisserian and meningeal infections, use penicillin. In diphtheria, use antitoxin plus penicillin. Penicillin has no curative effect in diphtheria as far as we have been able to see. But apparently there is no question but that it will cut down the carrier rate, if you give 240,000 units of penicillin a day through the acute phase of diphtheria. In tuberculosis, use streptomycin plus para-amino-salicylic acid. For gas gangrene, penicillin.

When you get down to certain of the gram-negative bacillary infections, as you can see, we cannot make out much difference clinically between the effects of aureomycin, chloromycetin, or terramycin. Actually none of them is very good in tissue infections produced by Bacillus proteus or by pyocyaneus. Of course, pyocyaneus responds beautifully to the polymyxins, but they show so much clinical toxicity that they will probably never be released for general use.

A curious thing about typhoid has been noted. Chloromycetin is the only one of these antibiotics that works. In the test tube aureomycin is almost consistently better as a bacteriostatic agent and terramycin is good, but for some curious reason, in the patient the only one of the three which works is chloromycetin. It is questionable whether any of the other Salmonella infections are affected by any of these agents. In tularemia, I would say from what we have seen in tick-borne tularemia (we have not had any rabbit fever lately to treat) that there is no difference between the therapeutic effects of chloromycetin and aureomycin. In brucellosis, we have seen no difference between the therapeutic effects of the three antibiotics. They are all good if given in proper doses. Personally, I prefer aureomycin.

In Listerella infections, which are very rare, we know that aureomycin is effective. In influenza meningitis, if you can give the chloromycetin to the child by mouth in adequate doses, it would be the method of choice for the treatment of this disease. If the baby cannot take this drug by mouth and you want to give something intravenously, then you should give aureomycin plus sulfadiazine (given separately). In chancroid, where you want to use an antibiotic, aureomycin and chloromycetin will be effective. These lesions can be cured by a few cents' worth of a sulfonamide, and all will agree that antibiotics cost just a little more.

All three of these new antibiotics will cure syphilis, but we do not know how well they will do it in comparison with penicillin. A matter of a year or two more has to elapse before we can begin to say which is the best for syphilis when one plans to use one of the three new antibiotics. We do not know about their use in the treatment of other types of spirochetal infection.

In granuloma inguinale, one may have to treat patients for three or four weeks before obtaining the results expected.

In Bartonella infections, use chloromycetin.

In streptobacillary infections, use streptomycin. We have not seen any of these cases lately, and we do not know what aureomycin, chloromycetin, or terramycin will do. I believe they will be effective, but these are rare conditions.

In rickettsial infection, all three appear very definitely to be effective. So far as rickettsial infection is concerned, you do not have to worry. Most of you will remember Dr. Zinsser's book on "Rats, Lice, and History," and you will remember that he pointed out that the greatest worry the louse has is thinking that some day he will crawl on some human being who has typhus, because if the louse crawls on someone who has typhus and bites him, the louse will die. Only one-third of the nonnative Caucasians who are bitten by the typhus-infected lice die, but every louse which bites a typhus patient dies. So, of course, the louse is scared to death of typhus. But recently it has been shown very clearly by controlled experiments that if you feed an infected louse on some blood which has aureomycin in it, you can cure the louse, too.

Now let us consider the viruses for a moment. Note psittacosis and lymphogranuloma venereum, which we know belong to the same group of large viruses. They respond very well to aureomycin and chloromycetin, and probably will to terramycin.

For primary atypical pneumonia it is somewhat difficult to make a distinction, but it is our impression that, in the dosage we have recommended, aureomycin is much more effective than either terramycin or chloromycetin in this disease. But let me say that that is only our opinion because it is practically impossible with this disease to set up a comparative control study which might give really good data.

In herpes zoster we have seen very good results in Baltimore, in most cases. Physicians in England, I found, were not so kindly disposed to either aureomycin or chloromycetin in this disease. They have not had as good results.

Then, as we go down the list, you will note that after herpes simplex I have left a blank, because I know that today I will hear many discussions between ophthalmologists, some of whom will say that the new antibiotics are good in herpetic infections of the eye, and others of whom will say that they have not had any success with them. Experimentally, one cannot show anything. It is easy to produce herpes in the eye of the rabbit, but the rabbit is one of the worst animals to work on with the new antibiotics, and to date all tests have been negative.

I should like to mention just one or two other items of interest in the treatment of infections with antibiotics. We do not know about chloromycetin, but we do know that aureomycin and probably terramycin are the most effective drugs that have yet been devised for the treatment of amebic infection. From the tropical countries, reports are coming back constantly of the excellent effect of these drugs in treating this type of infection.

Another interesting observation is that Trichomonas vaginalis generally re-

sponds to aureomycin after everything else has failed and the poor patient is almost frantic because of the discomfort caused by the disease. If the contents of a capsule of aureomycin is insufflated into the vagina two or three times a day, patients will show marked improvement in twenty-four to forty-eight hours, and in about a week or ten days will be cured. This disease is very common, and it is very disagreeable when severe. It is interesting that aureomycin has an effect in it. I don't know whether terramycin would be effective, but I think it probably would.

I have said practically nothing about streptomycin because Dr. Romansky and others have shown that a considerable percentage of strains of the gram-negative micro-organisms that are being isolated from infections are quite resistant to streptomycin. This is due to the fact that the originally susceptible organisms become resistant by throwing off mutants which are highly resistant. As many of these organisms are becoming resistant to streptomycin, I would not hesitate to say that, in this country today, I think we ought in general to limit the use of streptomycin to the treatment of tuberculosis because the chances of encountering resistant organisms, or making them resistant, are great.

TABLE II — THE PROPHYLAXIS OF INFECTIONS WITH ANTIBIOTICS

INFECTION OR CONDITION	PENICILLIN G	STREPTOMYCIN AND DIHYDROSTREPTOMYCIN	AUREOMYCIN	CHLORAMPHENICOL	TERRAMYCIN
Agranulocytosis	IB		IA	N	N
Gonorrhea and Gonorrheal Ophthalmia	IA		N	N	N
Syphilis	IA		N	N	N
Hemolytic Strep. Infection	IA		IB	N	II
Meningococcal Meningitis	IA		N	N	N
Puerperal Sepsis (Local and Systemic)	IB		IA	N	N
Rheumatic Fever	I		N	N	N
Subacute Bacterial Endocarditis	IB		IA	N	N
"Clean" Surgery	IB		IA	N	II
Colonic Surgery		IIP.O.+S.S.	IA	II	IA
Pulmonary Surgery	IB		IA	IB	IB
Established Surgical Infections	I°A	I°A	I°A	I°A	I°A
Extraction of Teeth	IB		IA	N	N

N—Not evaluated
IA—First Choice
IB—Second choice
II—Effective
S.S.—Sulfasuxidine
o—As indicated
Blank—Not effective
Postoperative

We have relatively nontoxic, good antibiotics for most of the infections in which we might use streptomycin, so why not employ them. I think one can say, therefore, "Use streptomycin only in tuberculosis, and then only when it is indicated."

I just want to point out a few things in table II which are of interest because the prophylactic uses of the antibiotics are increasing year by year as physicians become more experienced. Most of you have probably seen this table be-

fore, but the fact is that aureomycin (and I think terramycin will turn out about the same way) has been extremely helpful in cutting down the small residual of puerperal morbidity from infections which we have experienced in Baltimore. It is very easy to give and it is highly effective as a prophylactic agent in the prevention of puerperal sepsis. I am sure that you gentlemen, especially those of you who are otolaryngologists, have more experience with aureomycin as a prophylactic than I have, and that you will agree with me that its administration for preventive purposes is much easier on the patient than an injection of penicillin.

This is the third year that we have been studying aureomycin and chloromycetin. Year by year we have cut down our dosage requirements in respect to aureomycin. We have listed in table III our current dosage recommendations for the newer antibiotics. We have found that we can cut down markedly in relation to aureomycin, as I have just said. These doses shown in the table are about 50 per cent less than those I suggested two years ago for aureomycin. We have not been able to do this with chloromycetin. As soon as we try to cut down the dose of this antibiotic, our results have not been comparable with those obtained before. These are the suggested dosages for infections of varying severity. The doses of terramycin are tentative and subject to change, but we think they represent pretty well what a patient should receive who is moderately or severely ill with an infection.

TABLE III — DOSAGE SCHEDULES FOR AUREOMYCIN, CHLORAMPHENICOL AND TERRAMYCIN

SEVERITY OF ILLNESS	AUREOMYCIN		CHLORAMPHENICOL		TERRAMYCIN	
	INITIAL DOSE MG./KG. BODY WT.	TOTAL DAILY MAINTENANCE DOSE MG./KG. BODY WT.	INITIAL DOSE MG./KG. BODY WT.	TOTAL DAILY MAINTENANCE DOSE MG./KG. BODY WT.	INITIAL DOSE MG./KG. BODY WT.	TOTAL DAILY MAINTENANCE DOSE MG./KG. BODY WT.
Moderate Oral Route	None	20-30	60	60	None	25-50
Severe Intravenous Route*	5-10	20-40			5-10	20-40
Severe Oral Route	10	50	60	60-120	15	50-75

When the oral route of administration is being used, the calculated total daily maintenance dose is divided into four or three parts and is given at intervals of six or eight hours. The higher doses are recommended for infants and children under 4 years of age.

*When aureomycin or terramycin is being administered by the intravenous route, do not give more than 500 mg. in any single dose. The intravenous doses should be spaced at intervals of six to eight hours. A shift should be made to treatment by the oral route as soon as such is feasible.

The usual prophylactic dose of these antibiotics for ambulatory patients is 1.5 to 2.0 grams per day.

I will go over only the toxic reactions which relate to the new antibiotics, because everyone is familiar with the toxic reactions incident to the administration of penicillin and streptomycin (table

TABLE IV — IMPORTANT TOXIC REACTIONS RESULTING FROM ANTIBIOTIC THERAPY

REACTION	PENICILLIN	STREPTOMYCIN AND DIHYDROSTREPTOMYCIN	AUREOMYCIN	CHLORAMPHENICOL	TERRAMYCIN
Anaphylactic Shock	Very Rare	Very Rare	0	0	0
Skin Eruptions	Common	Common	Rare	Rare	Rare
Other Allergic Reactions	Common	Common	Very Rare	Very Rare	Very Rare
Drug Fever	Common	Common	Very Rare	Very Rare	Very Rare
Renal Injury	0	0	0	0	0
Anemia	0	0	0	Reported	0
Granulocytopenia	0	0	0	Reported	0
C.N.S. Injury	Very Rare	Reported	0	?	0
Vertigo	0	Common	0	Reported	0
Deafness	0	Occurs	0	0	0
Nausea	0	0	Occurs	Occurs	Occurs
Vomiting			Not Common	Not Common	Not Common
Loose Stools			Common	Common	Common
Mucous Membrane Lesions (Oral Administration)	Common	0	Occur	Occur	Occur
Secondary Lesions Due to Yeasts	Occur		Occur	Occur	Occur

IV). As you know, true allergic skin rashes and skin eruptions are rare. Drug fever is very rare. It is interesting that with chloromycetin you can get occasionally a mild hemolytic anemia in certain patients. While there have not been, to my knowledge, any cases of true agranulocytosis reported in the literature, definite instances of granulocytopenia have been reported, and studies of bone marrow have shown certain arrests in the maturation of formed elements in the marrow. I believe that one should check the white blood cell count at least biweekly when one is administering chloromycetin to a patient.

Vertigo, but not deafness, has been seen a number of times in patients taking chloromycetin, so that it is a thing one has to bear in mind. One doctor's wife of whom I know had vertigo for three months after she had taken chloromycetin.

Nausea is quite common with the newer antibiotics, especially if you take large doses of them. I suspect that the nausea is very much like that in a woman who has nausea of pregnancy. I think so because, when I took heavy doses of one of the newer antibiotics, I suddenly developed a great yen for pickles, sardines, crisp fried cold bacon, and cold corned beef right out of the can. As a matter of fact, that is all I ate for about two weeks. And I drank ice cold pasteurized milk with each dose of the antibiotic which I was taking.

I found—and I was glad to see that my friends at the Mayo Clinic had confirmed it in the next *Newsweek* that I

read — in my series of one patient (P.H.L.), in which I studied nausea very carefully (and maybe I was kidding myself), that, if one took the aureomycin (I gave myself away) with a glass of ice cold milk and then took a little ice cold milk all along the twenty-four hours, one felt very much better than when he did not drink the milk.

Vomiting is not too common unless the doses are large and the patient is expecting it. Some people always will vomit. I think it best not to allow a patient up and around if he is nauseated; I think he is much better in bed. Either cut down the dose, or keep him in bed. If patients are up and around, the chances that they will start vomiting are greater, and, once they start, your plan of therapy may well be ruined for the time being. You would then have to stop and start all over again.

Loose stools are quite common. It is a very interesting thing about the stools when one is taking one of these three new antibiotics. Very quickly the bacteria in the stool are suppressed in varying degrees. From the work which I saw in Stockholm — which was beautifully done — of the three antibiotics aureomycin has the greatest effect in suppressing the intestinal bacteria. When the bacteria are suppressed, one frequently finds an overgrowth of yeastlike organisms, such as Monilia, or Proteus or Pyocyaneus, which are resistant organisms. Concomitant with that overgrowth of yeastlike organisms, you may have skin lesions produced by Monilia. You may also have mouth lesions which are produced by Monilia. Don't be too certain, when you see patients with mouth lesions who are taking aureomycin or chloromycetin or terramycin, that those lesions represent a vitamin B deficiency. Just remember about the Monilia.

Then there is another thing about these drugs which is important to remember, especially for otolaryngologists. Patients with bronchiectasis or lung abscesses should not be treated for indefinite periods, because, with the suppression of the bacterial flora of the lesions, Monilia may become implanted and a pulmonary moniliasis may develop. This is a serious disease.

Other types of oral lesions may occur on any mucous surfaces. Whether these lesions are due to a vitamin deficiency is difficult to say. Notwithstanding, I believe that every patient who is getting more than 2 grams a day of any one of the newer antibiotics ought to have his daily requirements of the B complex administered as a supplement. If you want to give him more, it won't hurt him although it will probably be wasted, but he ought to have at least the daily requirements because such profound changes take place—and we really know very little about all the fine balance which is maintained and the nutrient factors which may be produced—in the course of bacterial metabolism in the stool. Until we know a little more about where we are actually going, I believe that this is the wise thing to do, because some very definite cases of B deficiency have developed.

Well, what has all this done? What has happened to some of our infectious diseases since we have had the sulfonamides and the antibiotics? I should like to report a few of the facts which are derived from mortality tables in this country.

What has happened to the mortality rate from lobar pneumonia in the last fifteen years. The rate really began to fall off the year that sulfapyradine became widely used, and it continued falling pretty well until penicillin was introduced. Then it had another sharp drop. I would predict that 1950 will show another sharp drop because of the introduction of the newer antibiotics. That is a pretty good record, but really we

ought to get it down to a mortality rate of 7, and not have it around 14 per 100,000, as it is currently.

The situation in respect to mortality from septicemia is extremely interesting, because you could argue, if you wanted to, that the introduction of the sulfonamides increased the death rate from blood poisoning, but I don't think it really did. It made the reporting of deaths from septicemia more accurate, so an apparent increase was noted in the mortality rate from this cause. But actually that is another matter. We really did not begin to get good results in our attempts to prevent deaths from septicemia until we used penicillin. Since then the mortality rate has taken a very sharp drop. I imagine that it will continue to fall sharply now that we have aureomycin, chloromycetin, and terramycin.

The curve for bacterial endocarditis is interesting. Here again the curve followed the trend line until penicillin was introduced, when it dropped sharply, and I think that the mortality will drop off again quite appreciably since the introduction of the three newer antibiotics.

The mortality rate of osteomyelitis is rather pretty because, after all, the common causes of osteomyelitis are Beta hemolytic streptococcal and staphylococcal infections. You would expect it to fall as soon as sulfanilamide was introduced, and of course with the introduction of thiazole and the diazines, and then with the introduction of penicillin you would expect it to fall rapidly. In Baltimore we rarely see cases of acute osteomyelitis at the present time. Where we used to see dozens of them in a year, we now see one or two a year, and the mortality rate is almost down to zero.

The next rate which I will discuss will be that from diseases of the ear and mastoid. I will pretend that I am not talking to otolaryngologists but that I am talking to internists or to general practitioners. When I discuss this rate, I always say that it illustrates why hearing has become such an important thing in the minds of the otolaryngologists. There just aren't many mastoidectomies to be done. But you know far better than I what is happening in the field of mastoiditis, both acute and chronic. It really is a startling thing when you consider that the chiefs in the large otolaryngologic services today say that often their residents are seemingly untrained because they have not had enough experience with a disease that we used to see a great deal; namely, acute mastoiditis.

This next mortality rate is really pretty. In 1948, only about sixty-seven people out of our population of roughly 150,000,000 died of scarlet fever, and about sixty-four were reported as dying of erysipelas. If one carries the mortality rate figures to two decimal places, he discovers a zero mortality in scarlet fever and erysipelas, and I think that for all practical purposes we have arrived at zero mortality for these diseases. I don't doubt that, within the next two or three years, certain other acute infections whose mortality rates are now down to a tenth of one per cent will also drop into this category.

Somebody said to me about three weeks ago, "What are you going to do now? Doctors are curing almost all of the infectious diseases. There will be new antibiotics but you will never have any five come along like penicillin, streptomycin, aureomycin, chloromycetin, and terramycin, which have made such a difference in the practice of medicine. Aren't doctors working themselves out of their jobs?"

I said, "Well, you ask me what doctors are going to do. I will tell you what I hope to do. I would like to retire in another nine years because, gentlemen,

if you think back, this has been one of the most interesting fifteen years in the history of medicine." You have seen from what I have said that if we can get something that is really good in tuberculosis and possibly in certain of the viral diseases, we are going to wipe out the mortality, and a certain amount of the morbidity, from these various diseases, and very few people will be dying of infections. It seems quite possible that, within the next four or five years, infections, as a specialty, which has been many physicians' interest all their years, will not be very important or interesting to young physicians. I recently asked our fourth year class how many of them were thinking of going into the field of infectious diseases. Not one of them held up his hand.

Symposium: The Collagen Diseases

THE PATHOLOGY OF COLLAGEN DISEASE APPLIED TO THE EYE

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FROM the time of Virchow, pathologists have generally limited their attention in microscopic pathology to the cellular changes occurring in organs and have ignored the reactions of the cellular and extracellular elements of the supporting connective tissue. It had been inconceivable to consider connective tissue in general and collagen specifically as being capable of producing any systemic disturbance when altered by a toxic agent. This oversight can generally be attributed to the attitude of viewing connective tissue fibers as an inert by-product of cellular metabolism with the sole function of serving as a structural framework for parenchymal cells. In addition, an awareness of the importance of an interfibrillary cement substance having a physiologic metabolic function and existing as a sensitive dynamic colloidal system was lacking. From gradual recognition of the viability of these extra parenchymal tissue elements and their ability to produce disease when disturbed has gradually evolved the concept of diseases of the connective tissue, generally referred to as collagen diseases. This includes among others, polyarteritis nodosa, lupus erythematosus, dermatomyositis, scleroderma, rheumatoid arthritis, rheumatic fever, and at least one ocular disease, scleromalacia perforans.[1,9,10]

Collagen, along with the reticular and elastic fibers, is the basic structural element of all connective tissue. Its structure may be considered as twofold; first, there are individual fibrils and bundles of fibrils, and secondly, these fibrils are cemented together by a physiologically active cement substance. This cement substance and the chemically similar amorphous ground substance lying between the bundles and cells is of great importance. Its chemical composition is not known other than that it is a mixture of mucoproteins and mucopolysaccharides, of which hyaluronic acid is one. As yet its possible biochemical function has not been determined, but Klemperer and his colleagues[10] have postulated the theory that this substance acts as the site of transfer for tissue metabolites and that it may be the medium of ionic interchange in the regulation of salt and water balance.

If the above hypothesis is correct, it is apparent that pathologic alteration of the ground substance would seriously impede cellular metabolism and readily account for the profound changes seen in diseases of the collagen tissue. It is also apparent that diffuse biochemical disturbance of this ground substance can produce serious systemic disease with minimal alteration in the minute tissue anatomy as seen in the micro-

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scope. This is best demonstrated by the subtle histopathologic changes only recently recognized in acute disseminated lupus erythematosus.

Collagen occurs intercellularly in all tissue, being an integral part of the fibers supporting and separating parenchymal cells and capillaries. It is in the walls of blood vessels, linings of the pleural, pericardial, peritoneal, and joint cavities, and in the eye as well as in the skin and subcutaneous tissues. It is present in all coats of the eye and represents the bulk of the cornea and sclera. In diseases of collagen tissue the site of pathologic alteration can be local, diffuse, or disseminated. This wide diversity in distribution is one of the notable characteristics of collagen diseases and at least partially accounts for the great variations in their symptoms, signs, course, and prognosis.

Thus, it is apparent that the site and extent, as well as the character of the injurious agent, determine the trend and peculiarities of any of the connective tissue diseases in a given patient.

The pathologic changes in the collagen diseases may not always be microscopically visible. However, when they are visible there is a common basic pattern despite apparent dissimilarities in the histologic picture. In some instances, with attempted repair there is proliferation and an increase in tissue bulk, as in scleroderma; and in others necrosis and loss of tissue mass are predominant, as in scleromalacia perforans. The term commonly applied to this basic reaction is "fibrinoid degeneration," which may occur in other disturbances as well. Normally collagen appears as variable-sized bundles of straight or wavy parallel fibrils appearing striated in the longitudinal axis and granular on cross section. These bundles stain pink with hematoxylin and eosin and blue with the Mallory trichrome stain. They vary in both size and shape depending upon the tissue in which they occur and extend in all directions, but unlike reticulin fibers, show no tendency toward branching. Scattered between the strands are cells that have the characteristic cytologic appearance of fibroblasts which are associated with but not directly connected to the collagen bundles.[14]

In fibrinoid degeneration there is an initial alteration of these collagen fibrils and ground substance followed by proliferation of fibroblasts and an infiltration of histiocytes and leukocytes. There may be simply alteration of the ground substance alone, characterized histologically by an increased eosinophilic staining and thickening of the tissue mass. Microscopically this resembles plasmoid edema fluid and is accompanied by loss of the wavy appearance of the fibrils and an increased refractility. Such change may be due to a deposition of deeply staining eosin substance between the fibers, or, more likely, an alteration in pH and an increased water content of the ground substance. If extensive in distribution, the clinical effect can be profound and far out of proportion to the apparent histologic tissue damage when such damage is limited to alteration of the ground substance alone. When more intensive, there may be dissolution of the fibrils as well, and in most severe reactions there are cellular changes in which chromatolysis of the cells and suffusion of basophilic nuclear material into the ground substance and tissue spaces occurs.[9,10,11]

The differentiation of the collagen diseases is dependent to a large extent upon the type of reaction as well as the distribution. In polyarteritis nodosa the primary vascular changes are segmental. They may range from simple swelling of the ground substance to complete necrosis with an inflammation involving the entire wall of the affected vessel (fig. 1). There may be an irreversible obliteration of the lumen of the vessel, or

with fibrotic repair of the damaged wall, recanalization and/or aneurysmal dilatations may follow. In lupus erythematosus, scleroderma, and dermatomyositis the morphologic changes may consist of conspicuous alterations in the walls of the smaller arteries and arterioles, in the skin, renal glomeruli, and endothelial connective tissue of serous membranes. There is swelling of the normally invisible ground substance and fibrinoid degeneration in the collagen fibers, which in the vessels encroaches on the lumen and may produce all degrees of obstruction. There may be foci heavily infiltrated with polymorphonuclear leukocytes, lymphocytes, and fixed connective tissue cells. Fibroblasts and histiocytes usually show degenerative changes such as pyknosis and nuclear fragmentation. Essentially the entire disturbance may be due to alteration of the connective tissue substrate in the vessels and capillaries, and the degree is dependent upon the extent of the dissemination as well as the intensity of the necrotic process. In the glomerular capillaries of the kidney this fibrinoid swelling may involve the basement membrane, producing discrete rigid glomerular loops commonly referred to as wire loop appearance, and this is particularly characteristic of lupus erythematosus.[2,11,16]

The eye is involved directly in collagen disease by primary insult of the ocular coats or vessels, either as an isolated focal disturbance or as one of multiple sites in a generalized process. Primary lesions occur in the cornea, sclera, retina, and uveal tract. The cornea is least often affected, but it seems possible that the so-called corneal ulcers occasionally seen in acne rosacea are in reality focal areas of fibrinoid degeneration of the corneal collagen tissue. Microscopically these ulcers do not show the characteristic features of the classic corneal ulcers and infiltrates. Rather, there is a moderately well defined area

FIG. 1—Choroidal arterioles showing swelling of the ground substance and early inflammation in polyarteritis nodosa.

FIG. 2.—Scleromalacia perforans showing fibrinoid degeneration in scleral tissue.

FIG. 3.—Polyarteritis nodosa showing focal area of fibrinoid degeneration in sclera.

of stromal dissolution suggestive of focal hypersensitivity reaction.

Lesions of the sclera are not uncommonly associated with rheumatoid arthritis and are generally classified as scleritis or episcleritis. Lesions may also appear as isolated, sharply demarcated areas of focal necrosis which were originally described under the term scleromalacia perforans.[17] These can occur associated with or independent of rheumatoid arthritis, and here there is complete dissolution of the collagen fibrils with chromatolysis and suffusion of the basophilic nuclear material into the tissue spaces. The initial focal necrotic process is followed by an infiltration of both suppurative and nonsuppurative inflammatory cells in the surrounding area and tissues, giving the histologic appearance of an abscess. Scleral lesions have occurred in polyarteritis nodosa but are extremely uncommon[8] (figs. 2 and 3).

Uveitis in association with rheumatoid arthritis has long been recognized. In acute attacks, solidification of the aqueous not infrequently occurs, thus giving some index of the severity of damage to the capillary system. Histologically the inflammatory cellular reaction is nonsuppurative although tissue damage may be severe. This process is subject to remissions and exacerbations, with permanent damage following repeated attacks. This type of reaction is compatible with the general pattern of collagen diseases. Choroidal lesions also appear in polyarteritis nodosa, but essentially these arterial lesions are no different than those occurring elsewhere.[6,7]

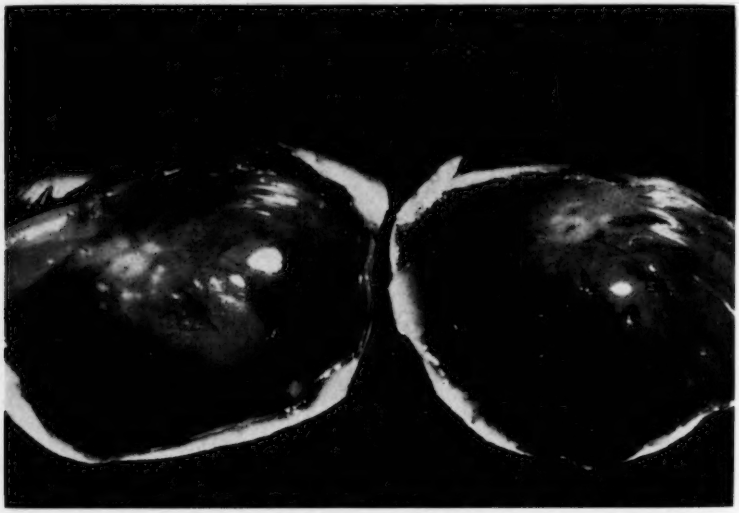

FIG. 4—Gross appearance of "retinal exudates" in diffuse collagen disease.

In the retina a characteristic "retinal exudate" simulating cotton-wool patches has been described as appearing in acute disseminated lupus erythematosus, dermatomyositis and polyarteritis nodosa.[3,4,12] This has been histologically identified as the cytoid body[13] (fig. 4). This cytoid body is in all probability a manifestation of fibrinoid degeneration involving neural tissue (figs. 5 and 6). The retinal vessels are also subject to involvement in the above diseases, which

FIG. 5—Lupus erythematosus showing cytoid body in retina.

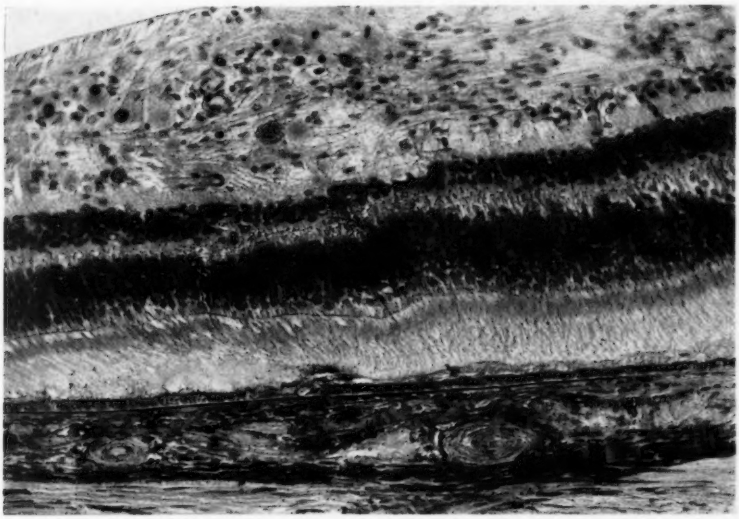

FIG. 6—Polyarteritis nodosa showing cytoid body in retina and fibrinoid degeneration in choroidal arterioles.

ranges from alteration of the connective tissue substrate alone to necrosis of the entire wall and occlusion of the lumen. Aneurysmal dilatation of the retinal vessels has been described in polyarteritis nodosa.

In conclusion, collagen may be considered as a structural tissue element normally existing as a dynamic colloidal system and probably subject to hormonal control. Pathologic alteration of this system by an etiologic factor such as hypersensitivity gives rise to an indeterminate group of systemic disturbances generally termed collagen diseases.[5,15] The eye having a high collagen content is occasionally involved in these diseases. The lesions are variable in type, site, and degree and the pathology of these must be considered the same as of those lesions occurring elsewhere in the body, modified by the peculiarities of the environment in which they occur.

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Symposium: The Collagen Diseases

CLINICAL OBSERVATIONS ON THE USE OF CORTISONE IN OPHTHALMIC DISEASES

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DURING the past fifteen years tremendous progress has been made in the knowledge of the hormones of the adrenal cortex. The chemistry of these hormones has been determined,[8-10,16] their effect on experimental animals has been studied by a host of investigators, the function of the adrenal cortex has been the subject of several exhaustive reviews,[1,5,6,17] and impetus has been given to the study of the effects of these hormones on the normal human subject and human beings afflicted with various diseases.

From the large mass of experimental, biochemical and clinical investigations it now seems established that the crystalline compounds isolated from the adrenal cortex belong to the "steroid" group of chemical substances[7]; that the hormones of the adrenal cortex are closely related steroid derivatives which have specific effects qualitatively different from one another[5]; that these compounds act mainly on electrolyte, protein and carbohydrate metabolism with some having the properties of sex hormones,[15] and that their most pronounced effect from a clinical standpoint has been among human beings suffering from disorders of the adrenal cortex.[11-14]

Our interest in the possible application of the adrenal cortical hormones to ophthalmology was stimulated by the clinical experiences of Hench, Kendall and associates in the treatment of rheumatoid arthritis with cortisone. Cortisone (17-hydroxy-11-dehydrocorticosterone) is but one of the group of corticosterones isolated from the adrenal cortex. It is sometimes referred to as compound E of Kendall. Utilizing this hormone Hench, Kendall and associates demonstrated a definite and remarkable alleviation of the symptoms of rheumatoid arthritis. When the hormone was withdrawn some degree of relapse occurred in most of their cases.

In ophthalmology it has been recognized for many years that some cases of arthritis are associated with anterior and posterior uveitis, scleritis and keratitis, and vice versa. Since the treatment of these ocular inflammations has been on a rather empiric basis, we were anxious to learn if the administration of cortisone would have as specific an effect on the ocular disease as had been demonstrated in the articular disease.

A supply of cortisone in the form of a suspension of its acetate was made available to us for investigative purposes in October 1949. We have allowed a year to pass before reporting the complete record of our patients, who probably were the first on whom the effect of cortisone in ophthalmic disease was studied. By allowing such an interval to elapse we felt that a more objective impression could be gained as to the short-term and long-term effects and the bene-

From the Section on Ophthalmology, Mayo Clinic.
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ficial, or detrimental, results of administration of cortisone in ophthalmic disorders.

To aid the reader in following the story of this investigation a summary of the cases studied is included. The case reports are arranged in the chronologic order of their observation, so that any evolution of thought or opinion concerning the efficacy of cortisone can be followed.

REPORT OF CASES

Case 1.—A white man, aged 51 years, had been a frequent patient at the Mayo Clinic since 1946 because of recurrent iridocyclitis of the right eye. He was known to have had six previous attacks of iridocyclitis in the same eye since 1929. We had had the opportunity to observe and treat the past four attacks occurring in 1946, February 1947, April 1947, and October 1947. Each of the past four attacks had been treated with intravenous injections of triple typhoid vaccine, instillations of atropine into the right eye and local applications of wet heat. Each of these attacks was brought under control by these means after two to three weeks, but with the resolution of each attack there was further formation of posterior synechias and reduction of vision. A diagnosis of rheumatoid arthritis and rheumatoid spondylitis also had been made during the summer of 1949.

The attack of pain, redness and blurred vision of the right eye that brought the patient under our observation on October 5, 1949, was of thirty-six hours' duration. The suspected recurrence of iridocyclitis of the right eye was confirmed on ocular examination. A mild circumcorneal flush was visible, and several pigmented cells were seen with the slit lamp, moving in the aqueous current. Heavy posterior synechias represented the residuals of past attacks. The visual acuity of the right eye was 6/13 with correction.

Intramuscular injection of cortisone acetate, 100 mg. daily, was commenced on October 6. After twenty-four hours from the first injection the ocular pain had disappeared. On October 9, after the patient had received 400 mg. of cortisone in four injections, administration of the hormone was discontinued because the pigmented cells in the aqueous had disappeared, the circumcorneal flush had vanished, and the visual acuity had improved to 6/7 with correction. No atropine was instilled into the affected eye during this four-day period of investigation.

Six and a half months then passed without the patient having any ocular difficulty. On April 26, 1950, the iridocyclitis of the right eye recurred. Because this attack was similar, from the standpoints both of severity and of duration of symptoms, to the one that had been under investigation during October 1949, we decided to withhold cortisone, treat the eye with our usual therapeutic devices for mild attacks, and thus have the attack of April 1950 serve as a control.

On daily instillations of atropine and local applications of hot fomentations the ocular symptoms became worse and the visual acuity decreased. After two weeks of this therapy injection of cortisone acetate was started; the atropine and hot fomentations were discontinued. By this time a circumcorneal flush of moderate degree was visible in the affected eye and about 20 cells per low-power unit field of the slit lamp beam were present in the aqueous. From both objective and subjective standpoints the eye seemed worse than at a comparable time when administration of cortisone was started for the previous attack in October 1949.

Cortisone acetate was administered in successive daily doses of 200 mg., 100 mg., 200 mg., 100 mg., 100 mg., 200 mg., 100 mg., 100 mg., 100 mg., 100 mg., 100 mg., and 100 mg. every second day thereafter until a total of 2 gm. in seventeen injections over a period of twenty-six days had been given. The intraocular inflammatory process seemed to get worse in the first several days after injection of cortisone was started, and it was necessary to reinstill atropine in the affected eye because of pain. Gradually the congestion, the "aqueous flare" and the pigmented cells in the aqueous disappeared after the sixth day of therapy. No additional posterior synechias were noted after the attack had resolved.

The patient then was free of ocular discomfort for eighteen days. On June 23 a recurrence of pain and redness in the right eye occurred and the patient instilled atropine for a period of three days. When we examined him on June 26, a recurrence of the iridocyclitis of the right eye was confirmed. Visual acuity was 6/12, right eye, with correction. Instead of cortisone being given by the intramuscular route again, a 2.5 per cent suspension of cortisone acetate* was prescribed for topical instillation in the affected eye, 1 drop every hour during waking hours. A 1 per cent solution of atropine was also instilled in the eye once daily. Because of improve-

*Provided through the courtesy of Dr. J. M. Carlisle, Medical Director, Merck & Co., Rahway, N. J.

ment in the ocular disease the administration of atropine was discontinued ten days later, July 5. The administration of cortisone was discontinued on July 8, 1950. Visual acuity was 6/6, with correction.

Three months have now passed without the patient noting a recurrence of the ocular disease.

In this case, our first under study, we were rather amazed at the prompt resolution of the inflammatory process within four days from the time cortisone was administered. We felt reasonably certain that cortisone was responsible for the ocular improvement, for no other systemic or local therapeutic agent was administered. Of course, it is possible that this attack would have come to a spontaneous resolution without any treatment, but it is unlikely to have done so in view of the duration of the previous attacks in this patient and the presence of extensive posterior synechias.

When the ocular disease recurred six and a half months after administration of cortisone was stopped we had become cognizant of the fact that cortisone did not bring about a final arrest of the ocular inflammatory process in many patients with an arthritic diathesis. This recurrence was utilized as a control in that cortisone was withheld and the disease was treated by our usual means. The fact that the disease became worse added further evidence that cortisone was responsible for the improvement of the attack during October 1949.

The response of this recurrence to cortisone, when administration was commenced two weeks after onset of the ocular disease, was much slower than in the first attack under investigation. It would seem from these data that cortisone, like many other hormones and chemicals used in therapeutics, exerts its most beneficial action when given early in the acute phase of the ocular disorder.

When the patient underwent a second relapse of ocular disease following the second series of intramuscular injections of cortisone it was gratifying to learn of the efficacy of combined topical administration of atropine and cortisone. In the future it may be possible to minimize symptoms or suppress the ocular disease by topical treatment only and thus obviate the risks of prolonged or repeated intramuscular injections.

Case 2.—A white woman, aged 55 years, reported to the clinic on October 15, 1949, because of redness and mild discomfort of the eyes of about three weeks' duration. On examination of the eyes a visual acuity of 6/10, each eye, with correction was noted. Congestion of moderate degree was evident in each eye. This congestion had a slightly violaceous hue. The results of ophthalmoscopic examination were essentially normal. Slit lamp examination revealed a few pigment cells moving in the aqueous. A diagnosis of bilateral scleritis was made.

This patient had had intermittent pains in the joints of the knees, feet, hips, neck and fingers since November 1948. These articular pains had become worse in spite of treatment with salicylates, applications of heat and physical therapy. During January 1949, a diagnosis of rheumatoid arthritis had been made at the clinic. At the time of the onset of the symptoms in the eye the patient stated that she was reasonably free of severe pain so far as the joints were concerned.

On October 15, cortisone therapy (100 mg. daily) was commenced. After two injections we noted some diminution of the congestion of the sclera of each eye. By the time ten injections (a total of 1 gm.) had been administered the scleral congestion had completely subsided and the patient estimated a 60 per cent improvement in articular symptoms. The sedimentation rate, which was 29 mm. per hour (Westergren method) at the start of the therapy, remained unaltered at the end of the ten-day period of treatment. Injection of cortisone was discontinued.

On the ninth day following the discontinuance of injection of cortisone the scleral congestion returned and the patient noted a recurrence of articular symptoms. By the sixteenth day the congestion had increased in degree so that the eyes appeared about the same as noted on the examination prior to cortisone therapy. The sedimentation rate was 65 mm. per hour.

On November 10, a second series of daily (100 mg.) injections of cortisone was started. In this second series nine injections (a total of 0.9 gm.) were necessary to free the eyes of their scleral congestion. The sedimentation rate dropped to 29 mm. per hour. Again injection of cortisone was discontinued.

Seven days after the completion of the second series of injections of cortisone the eyes again became congested and on the ninth day the articular symptoms became worse. The sedimentation rate was 61 mm. per hour.

On December 5, a series of daily intramuscular injections (4 cc.) of cholesterol was started. Because cholesterol is so similar in appearance to the suspension of cortisone acetate, we administered this preparation as a control, the patient thinking that injection of cortisone was recontinued. The symptoms in the joints and eyes became worse. A sedimentation rate of 68 mm. per hour was noted after seven injections of cholesterol.

On December 17, 1949, a third series of daily (100 mg.) injections of cortisone was started. In this series it required only four injections (a total of 0.4 gm.) to fade the scleral congestion. Instead of discontinuing the administration of cortisone as on previous occasions we maintained the patient on a dosage of 100 mg. every third day throughout a two-week period. Such a dosage kept the eyes white. The arthritic symptoms seemed to respond more quickly to this therapy than the ocular symptoms. On February 3, 1950, injection of cortisone was discontinued. The sedimentation rate was 35 mm. per hour. A total of 3.8 gm. of cortisone was administered in the three treatment periods. No local ocular treatment or other systemic therapy had been attempted during the period of investigation.

On May 1, 1950, almost three months later, the patient was re-examined. It was found that she had maintained all of the improvement noted when treatment was discontinued. At the time of this report eight months have elapsed since discontinuance of treatment without a recurrence of ocular disease.

This was the first case under investigation in which the ocular symptoms were bilateral and approximately equal in severity. Each eye responded in similar fashion to the periods of therapy and was equally prompt in exhibiting evidences of relapse. The over-all duration of the scleritis from the time symptoms first appeared until the eyes remained free of congestion without treatment was about four and a half months. This duration is similar to that of many cases of untreated scleritis associated with rheumatoid arthritis or cases in which various types of nonspecific foreign protein therapy are used. It might be reasonably asked, then, if this hormone influenced the duration of the disease, and from the treatment schedule which was utilized the answer must be in the negative. However, if this hormone did not influence the duration of the disease process it certainly influenced its severity, for there was no associated uveitis, no tendency to form nodules, and the patient was free of pain during the treatment periods. It is interesting to speculate concerning the duration of the disease had the cortisone not been completely withdrawn after the first ten-day treatment period but, instead, had been given either in smaller daily doses or 100 mg. doses at less frequent intervals. That this adrenal hormone exerted a specific effect on this ocular disease seems certain from the definite suppression of symptoms when the hormone was administered and the recurrence of symptoms when the hormone was withdrawn. The administration of cholesterol (a control medication) during one period helped in evaluation of the subjective symptoms.

Case 3.—A white man, aged 28 years, reported to the clinic on November 7, 1949, because of recurrent attacks of iritis in the left eye. He stated that he had undergone about nine attacks of iritis in the left eye since 1940. For this ophthalmic disease he had received approximately twenty injections of triple typhoid vaccine and twenty-five injections of boiled milk. With each attack there had been progressive visual loss in spite of treatment. His left pupil had been atropinized since January 1949. The right eye had been amblyopic since childhood. Since June 1949, he had noted marked stiffness and moderate pain in the region of the thoracic segment of the spinal column, ribs and neck. Intermittent swelling of the right knee had been present since September 1949.

Physical examination revealed severe synovitis of the right knee. There was marked limitation of neck movements. The sedimentation rate was 22 mm. per hour. A diagnosis of rheumatoid arthritis was made.

On ocular examination a visual acuity of 6/60, right eye, and 6/120, left eye, was noted. The right eye was essentially normal except for the amblyopia. A slight congestion of the left globe was noted. Photosensitivity was minimal. About twenty dense precipitates were present on the posterior surface of the cornea. A definite "aqueous flare" was present, but individual cells were not seen on slit lamp examination. The iris appeared atrophic. Heavy posterior synechias involving most of the pupillary margin were evident. The pupil was fixed and widely dilated. An early complicated cataract was visible. The vitreous seemed moderately hazy. A diagnosis of recurrent severe uveitis of the left eye was made.

On November 18, 1949, the atropine that the patient had been instilling in the left eye was discontinued. Injection of cortisone (100 mg. daily) was commenced. About eight days later the pupil of the left eye began to react to light stimuli and the patient experienced twinges of pain in the eye when attempting to read. We attributed these symptoms to the wearing off of the atropine effect. Pigment cells slowly moving in the aqueous were noted for the first time by means of slit lamp examination. Atropine was again instilled daily.

On December 2, 1949, injection of cortisone was discontinued because we had failed to note any improvement in the left eye during the fifteen-day period. A total of 1.5 gm. of cortisone had been given. However, the marked synovitis of the right knee almost disappeared during this period of therapy.

In this particular case the ocular disease did not respond to the administration of cortisone as in the first 2 cases. It seemed to us that the eye showed no significant beneficial effects from the amount and duration of cortisone administration that was given to this patient. It might be argued that had the cortisone been given in larger doses or administered over a longer period there would have been some beneficial effect. It is true that the disease process was of greater severity in this case than in the first 2 cases and, therefore, might reasonably be expected to require either a larger amount of the hormone or a longer period of treatment. However, our impression gained by this two-week period of observation was that cortisone will have no appreciable effect in absorbing keratic precipitates of long standing, will not dissolve synechias, nor reverse the process of opacification in the lens. It seems probable that the eye would have shown some evidence of improvement had it been capable of it, for the disappearance of the synovitis of the knee seemed to indicate that cortisone was having a beneficial effect on the patient as a whole.

Case 4.—A white boy, aged 14 years, had been a patient at the clinic on several occasions since 1947, when a diagnosis of bilateral vernal conjunctivitis was first established. This boy, according to the parents, had had photophobia and itching of the eyes accompanied by a ropy discharge at intermittent intervals since 1944. In May 1947, November 1947, March 1948, and October 1948, this patient had received beta irradiation to the palpebral surface of each upper eyelid, each eyelid receiving a total dosage of 6 gram seconds in the four treatment periods. Because the boy's ocular symptoms did not recur during the spring of 1949, as had occurred during the spring months of every year since 1944, the parents did not bring the patient to us for therapy as instructed.

During October 1949, there was a marked exacerbation of all the ocular symptoms of vernal conjunctivitis with, in addition, a large ulcer on the cornea of the right eye. The ulcer would not heal with the usual methods of local therapy, and the large granulations on the palpebral surface of the right upper eyelid seemed to keep the affected area of the cornea denuded of its epithelium by the rubbing of the eyelid against the cornea. Antihistaminics administered topically and systemically were of no avail in alleviating the ocular symptoms. The lacrimation had become so profuse and the rubbing of the eyes so persistent that the skin of the face had become excoriated.

On November 25, 1949, intramuscular injection of cortisone acetate, 100 mg. daily, was commenced. After ten injections (a total of 1 gm.) had been given, the ropy discharge had almost entirely disappeared, the itching

had ceased, the epiphora subsided, and the excoriations on the skin of the face healed. The photophobia had abated somewhat so that the boy was able to read comic books, a privilege that had been impossible during the acute exacerbation. In spite of this marked subjective improvement, however, the size and appearance of the corneal ulcers and the granulations on the palpebral surface of the upper eyelids remained unchanged. No untoward systemic effects of the administration of cortisone were noted. We did not have an opportunity to observe or treat this patient beyond the ten-day period. Several weeks after he left our care we learned by letter that most of the ocular symptoms had returned and the granulations on the palpebral surfaces of the upper eyelids finally had been excised.

This was the first nonadult of our series of patients to receive cortisone. In the light of our present knowledge it seems possible to give a patient of this age much more cortisone than 1 gm. At the time of this investigation we were very cautious concerning the dosage that could be given to an adolescent. No untoward effects resulted from administration of cortisone to our knowledge. Instead, the apparent effects of this hormone seemed to be beneficial ones. The child had a feeling of well-being and, most amazing, the subjective symptoms of the disease abated. This improvement in one phase of the disease is all the more unusual when it is remembered that the granulations on the under surface of the upper eyelids appeared unchanged during therapy.

The rationale for the use of cortisone in such a disease of the eyelids is based on a rather theoretical premise. Although the cause of vernal conjunctivitis is not known, many ophthalmologists feel that the disease has some allergic basis because of its usual seasonal character and the ever-present eosinophils in the conjunctival tissues and secretions. The possible "anti-allergic" effect of cortisone and the favorable response of certain disorders associated with eosinophilia[4] to administration of cortisone prompted us to try this adrenal hormone in this disease of the eyelids. Our desire to investigate the effect of cortisone on such a disease was more fully realized in a subsequent case.

Case 5.—A white man, aged 27 years, requested an ophthalmoscopic examination on December 1, 1949, because of blurred vision in the left eye since November 20, 1949. He stated that the blurred vision seemed to occur about two days after the onset of a "head cold." He further stated that the visual acuity of each eye, to his knowledge, had always been 6/5.

On ophthalmic examination a visual acuity of 6/6 was noted in the affected eye, the left one. With the ophthalmoscope a fine, dust-like haze was visible in the vitreous of the left eye. With the slit lamp a few pigmented cells could be seen moving in the aqueous currents and a definite but slight "aqueous flare" was evident. A diagnosis of uveitis of the left eye was made.

A general physical examination was performed in the hope that some clue as to the origin of the uveitis might be uncovered. The only apparent abnormality was eosinophilia. Leukocytes numbered 5,800 per cubic millimeter of blood. A differential blood count revealed 30 per cent lymphocytes, 53 per cent neutrophils, 11 per cent eosinophils, and 6 per cent monocytes. The differential blood count was repeated several times to verify the presence of eosinophilia.

For a period of eight days this patient received a daily injection of 300,000 units of duracillin. From December 8 to December 22, eight intravenous injections of pyromen were given. This was followed by two intravenous injections of triple typhoid vaccine. The patient proved to be immune to the triple typhoid vaccine. By this time the left eye had become worse, with a decrease of visual acuity to 6/20 and an increase in the haze of the ocular media. From December 27, 1949, to January 6, 1950, five intramuscular injections of boiled milk were of benefit, for the visual acuity improved to 6/12 and the pigmented cells in the aqueous of the left eye definitely decreased in number. The haze in the vitreous persisted, however. Unfortunately, this patient acquired an immunity to the boiled milk and it was not possible to obtain a febrile response to additional injections. A series of seven intravenous injections of histamine was then given, but the eye did not maintain its improvement. On February 1, examination of

the left eye showed a visual acuity of 6/30. The vitreous had become very hazy and the aqueous seemed filled with slowly moving pigmented cells. The pupil had been maintained under full mydriasis during the treatment period. Leukocytes numbered 7,600 per cubic millimeter of blood. A differential blood count revealed 36 per cent lymphocytes, 36 per cent neutrophils, 23 per cent eosinophils and 5 per cent monocytes.

On February 2, intramuscular injections of cortisone acetate, 100 mg. daily, were commenced. After the patient had received the seventh daily injection the first objective improvement in the eye was noted. On February 10, leukocytes numbered 5,600 per cubic millimeter of blood. A differential blood count revealed 18 per cent lymphocytes, 72 per cent neutrophils, 2 per cent eosinophils and 8 per cent monocytes. On February 23, when twenty-two daily injections (2.2 gm. of cortisone) had been given, the visual acuity of the left eye had improved to 6/10 and only an occasional pigmented cell was visible in the aqueous current. Two more injections (100 mg. each) of cortisone acetate were given over a four-day period and injection of the hormone was then stopped.

Unknown to the patient, cholesterol then was substituted for the cortisone so that a controlled study was possible. After an interval of ten days of injection of cholesterol the left eye seemed to be getting worse, and after a period of two weeks we knew definitely that the uveitis was more active, for the visual acuity had decreased to 6/12 and there were many pigmented cells in the aqueous again.

A second series of intramuscular injections of cortisone (100 mg. daily) was started on March 13. Improvement was rapid. After five injections the veil of dust in the vitreous seemed to break up, and the opacities became conglomerate in several groups that swirled about in the vitreous as the eye moved. This second series of injections of cortisone was stopped on March 17, the patient having received a total of 2.9 gm. of cortisone in the two series of injections. By March 25, the visual acuity had improved to 6/7+ and the pigmented cells had disappeared from the aqueous. On April 1, leukocytes numbered 6,100 per cubic millimeter of blood and a differential blood count of 39 per cent lymphocytes, 41 per cent neutrophils, 15 per cent eosinophils and 5 per cent monocytes was found.

The patient maintained this state of improvement until April 25, when an immobile, dustlike haze was again noted in the vitreous of the left eye and pigmented cells were visible in the aqueous. The visual acuity, however, seemed little affected, remaining about 6/5. A third series of injections of cortisone (100 mg. daily) was started on April 25, 1950, and a total of 1.2 gm. (twelve injections) was administered. Again the ocular media cleared and there has been no evidence of a relapse in the five-month interval since treatment.

The puzzling feature of this case was the unexplained eosinophilia, which has persisted although the ocular disease has remained arrested for about five months. Whether the posterior uveitis was related to the eosinophilia is not known. The cause of this patient's ocular difficulty was never discovered.

In no other case of our series has the beneficial effect of cortisone been quite so gratifying, for the left eye of this patient, one of our physician colleagues, was steadily becoming worse in spite of our therapeutic efforts. Here again, as in cases 1 and 2, relapses occurred when the injection of cortisone was discontinued but after repeated courses an arrest or resolution of the inflammatory process seemed to occur. An explanation for the rapid response of the first relapse to administration of cortisone and the slow response of the second relapse to cortisone was not found.

Case 6.—A white boy, aged 8 years, was brought to the clinic on February 10, 1950. The mother of this patient stated that he had suffered from photosensitivity and itching of both eyes since the spring of 1946. At the onset of the ocular difficulty the symptoms were seasonal, being worse during the summer months than in other seasons, but in the past two years the ocular symptoms were equally persistent throughout all seasons of the year. Numerous allergy surveys and desensitization procedures had been carried out without bringing relief to the eyes. In January 1949, an unknown amount of beta irradiation was given to the palpebral surface of each upper eyelid. This therapy, as well as numerous "eye ointments" and "eye drops," failed to produce any apparent difference in the ocular symptoms.

On ocular examination a visual acuity of 6/20 was noted. The patient was so photophobic that the eyelids could hardly be sepa-

rated for inspection. When eversion of the upper eyelids was accomplished, a large number of thick, flat-topped papules were visible on the tarsal surface. The conjunctiva of the lower eyelids was moderately congested, and the tissues seemed to have a milky hue. A ropy mucoid discharge could be wiped away from the lower fornices of the conjunctiva. There was moderate congestion of the bulbar conjunctiva. The examination was interrupted by spasms of itching of the patient's eyelids. A diagnosis of severe vernal conjunctivitis was made.

On February 13, intramuscular injection of cortisone acetate, 75 mg. daily, was started. After six daily injections had been given, definite subjective improvement was evident. By February 27, fourteen injections had been administered (1.05 gm.). The patient had gained 6 pounds (about 2.7 kg.). Much of the itching had subsided, only a minimal discharge was evident, and the patient could go outdoors in the sunlight without dark glasses. Although the papules on the palpebral surfaces of the upper eyelids were definitely less congested, we could not be certain that there was any decrease in size.

Because of the marked gain in weight and rapid disappearance of the subjective symptoms the amount of hormone was reduced to 50 mg. daily. On this regimen the patient seemed to reach a plateau of improvement. On most days he was relatively symptom-free and carried on his school work with a tutor, but at irregular intervals he would be inconvenienced by a stuffy nose, a slight increase in itching, and photosensitivity. The papules were an estimated 20 per cent smaller. Because the disease seemed to be at a standstill, injection of cortisone was discontinued on March 21, 1950, the patient having received 36 injections and a total of 2.15 gm. of the hormone.

At this point cholesterol was substituted for the cortisone without the knowledge of the patient, it being our desire to use the cholesterol as a control medication for observing the subjective symptoms. Within four days after injection of cholesterol was started, all symptoms had recurred and the patient gave up his school work.

On March 27, a second series of intramuscular injections of cortisone, 75 mg. daily, was commenced. The first definite evidence of improvement appeared after ten injections had been given. The daily administration of this hormone was maintained and the improvement continued. The papules began to shrink and were replaced by stellate-shaped, white scars on the surface of the conjunctiva. The bulbar conjunctivas and the palpebral conjunctivas of the lower eyelids were normal in appearance. From a clinical standpoint the ocular disease had subsided. Although the electrolyte levels of the blood were still within the ranges of normal, we were worried that signs of hormone intolerance might soon appear because the patient's face was becoming paunchy and "moon-shaped." To forestall a possible recurrence of symptoms such as had occurred after the completion of the first series of cortisone given daily, rather than stopping the hormone abruptly, on May 18 the tapering-off period was commenced, the patient receiving 15 mg. less cortisone every fourth day. On May 29, the second series of cortisone injections was completed, the patient having received a total of 4.2 gm. in sixty-two injections. The combined total of the first and second series amounted to 6.35 gm. administered over a range of 106 days.

In spite of the marked resolution of the disease at the time the second series of cortisone injections was stopped, in four days the itching of the eyes re-appeared, in seven days the photosensitivity of the eyes and the milky hue of the lower palpebral conjunctiva became evident, and in ten days the ropy discharge and papules were reforming. A suspension of cortisone acetate, 8 mg. per milliliter, was instilled, one drop every hour in each eye daily while awake from June 9 until June 15. Administration of the cortisone drops was discontinued because there had been no noticeable effect on either the subjective or the objective symptoms. An ointment containing 25 mg. of cortisone per gram of base was substituted for the topical cortisone. Although the ointment seemed better tolerated by the patient than the cortisone drops there was no appreciable effect on the eyelids or eyes. After a six-day trial, administration of the cortisone ointment was also discontinued.

On June 20, a third series of intramuscular injections of cortisone, 75 mg. each, was started. This third series of injections of cortisone was given to prevent a too exuberant re-formation of the papules on the palpebral surfaces of the upper eyelids and to permit the irradiation of the palpebral conjunctiva with beta rays of radium without causing too much discomfort to the boy. During the fifteen injections of cortisone (1.12 gm.) from June 20 until July 8, the symptoms of the vernal conjunctivitis improved and the beta irradiation was completed. No more cortisone was given after July 8, 1950, and the patient was released from our care.

Altogether, in the three series of administrations of cortisone, this boy had received 7.47 gm. of cortisone by means of 113 injections over a period of 146 days.

From the standpoint of the age of the patient and the amount and duration of the administration of cortisone this is the most unusual and interesting case of the entire series. Throughout the entire period of observation we watched this boy as carefully as possible for definite evidence of intolerance. Except for the rounded contour of the face there did not seem to be any external manifestation of approaching intolerance to cortisone. The gain of weight accompanying the initial series of injections was combated with a reduction diet. The results of blood electrolyte studies remained normal. The follow-up period on this patient is exceedingly short considering the potency and duration of this hormone administration, so that it is possible some delayed effect of administration of cortisone may become evident.

This patient's ocular disease was as severe as the condition described in case 4 and it gave us an opportunity to confirm some of our impressions as to the effect of cortisone on vernal conjunctivitis. In both cases definite subjective improvement was evident in about seven to ten days, but the effect on the conjunctival pathologic changes was disproportionately slight. In case 6 it required about 3 gm. of cortisone given in a six-week period to bring about a pronounced and definite change in the size of the granulations. However, once the resolution commenced it was relatively rapid. When there was complete resolution of the granulations and the surfaces of the palpebral conjunctivas were smooth and flat it seemed almost miraculous to the parent who had lived with this boy through two years of ocular annoyance and distress.

Of course, the relapse of the disease after each series of injections of cortisone was a great disappointment to the patient, to his parents, and to us. The "tapering-off" period near the end of the second series of injections of cortisone was an attempt to forestall such a relapse and theoretically permit the adrenal cortex to resume its function while the cortisone was given in successively smaller doses.

This case also served as one of the few in the series for the evaluation of topical administration of cortisone in the form of "eye drops" and "eye ointment." In this case cortisone administered in this form was without effect. Perhaps, in a case of lesser severity such a method of administration would have helped.

Case 7.—A white woman, aged 54 years, returned to the clinic on March 24, 1950, because of pain and loss of vision in each eye of seven months' duration. This patient had been under observation previously at the clinic from November 1948 to March 1949, because of arthralgia and stiffness of the joints of the hands, elbows, knees, hips and ribs, as well as asthenia and a loss of 45 pounds (about 20 kg.) since June 1948. A diagnosis of rheumatoid arthritis was made during this observation period. The patient's arthritis improved to such an extent that she was permitted to return home and during the summer of 1949 carried on her housework to a limited degree.

Her ocular difficulty commenced in September 1949 and was characterized at onset by blurred vision and congestion of the eyes. The self-administration of aspirin, which had helped to keep the articular symptoms under control, did not influence the course of the ocular disease and the vision became progressively more blurred. Sometime during the fall of 1949, a dull, almost constant pain commenced in each eye.

On ocular examination a visual acuity limited to the ability to count fingers at a distance of 1 meter was noted. Severe congestion of each eye was evident. Tonometric tension was 35, right eye, and 41, left eye, Schiötz. With the slit lamp a pronounced "aqueous flare" was visible, pigmented deposits covered most of the posterior surface

of the corneas, and several posterior synechias were present in each eye. On ophthalmoscopic examination the media of the eyes proved too hazy to enable visualization of the details of the optic papillae. A diagnosis of bilateral uveitis and secondary glaucoma was made.

On examination of the joints there did not seem much objective evidence of disease. The sedimentation rate was 54 mm. per hour (Westergren method).

On March 29, 1950, intramuscular injection of cortisone acetate, 100 mg. daily, was started. By the time seven daily injections had been administered the congestion of the eyes had been reduced about 50 per cent, the visual acuity had improved, and details of the fundus were becoming evident on ophthalmoscopic examination. The intraocular tension continued to be elevated above the limits of normal. When twenty injections were completed on April 17, the right eye was free of congestion and only minimal congestion of the left globe was present. The keratic precipitates and posterior synechias seemed unchanged as compared to the examination prior to injection of cortisone. The media, however, otherwise had cleared to such a degree that the fundus of each eye was visible and appeared normal. The visual acuity had improved to 5/60, each eye. The intraocular tension was still greater than normal, right 44, left 36, Schiötz.

The daily administration of cortisone was continued, and on the following day, April 18, bilateral basal iridectomy was performed through keratome incisions in each cornea. This intraocular surgical procedure was accomplished without complication. Throughout the first postoperative week the eyes remained relatively quiet although a slight increase in the severity of the uveitis was evident on slit lamp examination. On April 24, six days after the ocular operation, the visual acuity was 6/60 in the right eye and 4/60 in the left eye. The intraocular pressure had dropped to 28, right eye; 11, left eye, Schiötz. The expected marked exacerbation of the uveitis as the result of the intraocular operation did not occur and the eye continued to be relatively asymptomatic through the subsequent postoperative weeks although minimal activity of the uveitis continued as determined by repeated slit lamp examinations.

On May 10, when forty-two injections (4.2 gm.) had been completed we decided to taper off the dosage of cortisone, for there seemed some physical and laboratory evidence of an approaching intolerance to the hormone. The patient's face had become puffy, the hair soft and silky, the skin soft and oily, and the serum potassium levels were approaching the lower limits of normal. No hirsutism was evident and the total gain in weight was only 3 pounds (about 1.4 kg.).

Every third day the dosage of cortisone was reduced by 15 mg. On May 27, the last cortisone was administered in the reduction schedule, the patient having received a total of 4.9 gm. in fifty-seven injections over a fifty-seven-day period of observation. Except for a few cells in the anterior chamber, a minimal aqueous ray, the old keratic precipitates, and a few additional posterior synechias, the eyes seemed reasonably free of uveitis. Visual acuity was 6/60, each eye. With a suitable correction for presbyopia the patient was reading the larger print in the newspapers and carrying on written correspondence.

By June 1, five days from the time when injection of the hormone was stopped, the congestion of each eye had returned to a marked degree although the intraocular tension remained normal. A second series of daily injections of cortisone (100 mg. each) was commenced on this day. When nine injections were completed the congestion of each eye had again disappeared although the uveitis still seemed in a smoldering stage as determined by the cellular content of the aqueous. At this point we discontinued the daily injection of cortisone and, instead, administered the hormone every other day and on several occasions every third day. We found that injections given every third day were not sufficiently frequent to maintain the uveitis in an arrested phase as determined by the lack of congestion of the eyes. Injections of 100 mg. every other day, however, seemed sufficient.

On June 23, the intramuscular administration of cortisone was supplemented by a suspension of cortisone acetate (8 mg. per cubic centimeter) in a diluent furnished by Merck & Co. and applied topically to the eye (1 drop, each eye, every hour except during sleep). This supplemental administration of hormone failed to clear the aqueous of cells, however. On June 29, the second series of seventeen injections of cortisone and the topical administration were discontinued. The patient had received a total of 6.6 gm. of cortisone by the intramuscular route by means of seventy-four injections in an observation period of ninety-three days.

In a period of nine days after the injections were discontinued the signs and symptoms of uveitis had increased to a degree similar to the severity of the inflammatory

process noted before injection of cortisone was started. Secondary glaucoma once again became a threat. Injections of nonspecific foreign protein, local instillations of atropine, and frequent applications of wet heat to the eyes kept the intraocular tension at a normal level, but the uveitis showed little tendency to improve. No further injections of cortisone were given.

The most noteworthy feature of this case was the accomplishment of an intraocular surgical procedure during the course of active uveitis without producing serious damage to the eye. Heretofore, we have never dared to perform a surgical procedure on an eye in the midst of an acute inflammatory process, for such manipulation would only produce an exacerbation of the inflammatory process and usually results in a further decrease of visual acuity. Even during the quiescent phases of recurrent uveitis, iridectomy is carried out with some trepidation because of the risk of reactivating the disease. In this case the postoperative course of the eye was unusually quiescent and had it not been for the cortisone we seriously doubt if such a surgical procedure could have been accomplished without undue risk to the eye. This surgical intervention succeeded in lowering the intraocular pressure, which had evidently been high for some time.

This patient exhibited the most severe uveitis of any person in our group of patients having intraocular inflammatory disease that received cortisone. The disease had also gone the longest time without treatment. It is interesting to speculate on the possible mode of action of cortisone when it is remembered that in three weeks severe uveitis that had gone unchecked for a period of seven and a half months was reduced to but minimal manifestations, yet by the continued administration of this beneficial agent the disease could not be brought to a halt.

In an attempt to arrest this ocular disease this patient received more cortisone (6.6 gm.) than any other adult of this series. Signs of approaching intolerance appeared when this woman had received approximately 4 gm. of the drug in a period of one and a half months.

In this case two methods were used to withdraw the hormone on the possibility of preventing a relapse. Following the first series of injections the "tapering-off" method, such as was described in the previous case, was utilized, and the injection of cortisone was given on alternate days as had been successfully tried in case 2. Neither method of withdrawing the hormone proved successful in preventing a relapse of the uveitis in this woman.

Case 8.—A white woman, aged 33 years, came to the clinic on February 21, 1950, because of gradual loss of vision in the left eye since January 14, 1950. She had been treated with injections of vitamin B complex three times weekly for three weeks shortly after onset of the eye difficulty.

Ophthalmic examination revealed a visual acuity limited to the recognition of fingers in the left eye. A slightly elevated gray area of chorioretinitis occupied the left macula. Visual field examination showed a central scotoma of 10 degrees diameter to be present with a nucleus dense to a 35 mm. white test object at 1 meter distance. The sedimentation rate was 7 mm. per hour (Westergren method). Physical examination failed to uncover any clue as to the origin of the ocular disease.

The patient was hospitalized for foreign protein therapy. After she had received three intravenous injections of triple typhoid vaccine in a six-day period with adequate febrile response there was no appreciable change in vision or alteration of the visual fields. This treatment was discontinued.

After observing the patient for several weeks without noting any significant change in the appearance of the lesion at the left macula, we began injection of cortisone acetate on April 11. On this day visual acuity in the left eye was recorded as 1/60. On each of the first two days the patient received 200 mg. of cortisone intramuscularly. Thereafter

100 mg. daily was given. After she had received eleven injections, or a total of 1.3 gm., injection of the hormone was discontinued. The lesion at the left macula seemed to become smaller and the scotoma on visual field examination appeared narrower in diameter during the treatment period, but the visual acuity did not improve.

This case was the first in which cortisone was administered because of a so-called chorioretinitis. Although the inflammatory lesion seemed to improve during the period of administration of cortisone, the improvement was not any greater than would have been expected had the lesion been untreated. We were of the impression that cortisone was of no definite benefit to this particular case. In assessing the value of cortisone, however, it must be remembered that the inflammatory process was of three months' duration when the hormone was first administered.

Case 9.—A white man, aged 22 years, came to the clinic on April 17, 1950, because of diarrhea, arthritis and blurred vision. He had previously been a patient at the clinic from May 15 until June 1, 1949, because of intermittent diarrhea of eleven months' duration and recurrent arthritis of nine months' duration. A diagnosis of chronic ulcerative colitis had been made on this visit. In December 1949 the patient had experienced an exacerbation of the articular and intestinal difficulties. Through January 1950 the articular symptoms had seemed to improve on a regimen of heat and rest. The number of bowel movements also decreased to about six a day during January.

In the early part of February, the left eye had become red and sensitive to light. The vision of the left eye became increasingly more blurred as the congestion and photosensitivity persisted. An ophthalmologist was consulted, and daily instillations of atropine in the affected eye were prescribed. In addition the patient took some capsules of aureomycin and was instructed in the application of wet heat to the left eye. When the eye failed to respond to such measures the treatment was supplemented by two injections of typhoid "H" antigen. According to the patient this additional therapy had resulted in no significant change in the symptoms of the eye.

Physical examination revealed that the chronic ulcerative colitis was still present. Two ulcers, each about 3 cm. in diameter, were noted on the posterior wall of the bowel on proctoscopic examination. There was limitation of motion of the right elbow joint to a moderate degree, with moderate pain when attempts were made to straighten the arm. An area of edema measuring about 5 mm. in diameter was grossly visible in the temporal half of the left cornea. With the slit lamp it was noted that the edema seemed confined to the substantia propria of the cornea. There was no vascularization of the lesion in the cornea, no erosion of the corneal epithelium overlying the area of edema was noted, and no cells in the aqueous currents were visible. Visual acuity of the affected eye was 6/15 with correction. A moderate degree of epiphora and photosensitivity was present. A diagnosis of keratitis of the left eye was made. The sedimentation rate was 37 mm. per hour (Westergren method).

Cortisone acetate was first administered on April 20, 1950. On each of the first two days 200 mg. was given intramuscularly and on each successive day thereafter 100 mg. was injected. On April 24, four days after this therapy was commenced, the photosensitivity of the affected eye had almost subsided, the edema of the cornea seemed to be fading, and the visual acuity was improved. The number of daily stools had decreased from six a day to two a day. On May 1, a visual acuity of 6/6 in the left eye, with correction, was noted.

On May 8, nineteen days after injection of cortisone was commenced, administration of the hormone was discontinued, the patient having received a total dose of 2.1 gm. A residual area of edema measuring about 2 mm. in diameter was visible only with the aid of the slit lamp in the temporal portion of the left cornea. The patient was free of ocular symptoms. The sedimentation rate was 19 mm. per hour. An estimated 85 per cent subjective relief and 95 per cent objective improvement in the articular difficulty was noted. Although the patient experienced only an average of two stools daily during the period of investigation, proctoscopic examination showed no measurable reduction in the diameter of the two ulcers in the posterior wall of the bowel as the result of administration of the hormone. The patient was observed daily for a period of two weeks after the injection of cortisone was discontinued. During this interval the edema of the cornea gradually subsided, so that it was no longer

visible by means of slit lamp examination. Four months after the injection of cortisone was stopped the patient reported that no recurrence of the ocular trouble had occurred.

This case was the first of 2 in which cortisone was administered because of the triad of ocular disease, arthritis and chronic ulcerative colitis. All of these three disease processes had been resistant to the usual therapies. The improvement in the ocular disease as the result of administration of cortisone was striking and complete; the improvement in the arthritis was also marked, but transient; whereas the chronic ulcerative colitis showed no significant objective improvement. This varied response of the three disease processes to cortisone would suggest that the eye is among the most responsive of the tissues and organs known to be sensitive to the administration of this particular hormone of the adrenal gland.

Case 10.—A white woman, aged 32 years, was sent to the clinic on April 26, 1950, because of diarrhea, arthritis and blurred vision in the left eye. The patient stated that she had experienced recurring bouts of abdominal cramps, fever and diarrhea since January 1950. During the early part of April there had been intermittent pain in the joints of the hands, wrists, ankles and neck. On April 12, pain, redness and blurred vision were noted in the left eye. On April 14, scopolamine was instilled in the affected eye, and this medication was repeated daily until April 25, when it was discontinued. During the interval of therapy with scopolamine the pain and congestion of the eye gradually disappeared, although some blurring of vision persisted.

Physical examination revealed chronic ulcerative colitis with the inflammatory changes involving the entire length of the colon but limited to the mucosa. Swelling and tenderness in the tarsal area of the right foot were noted. Subastragalar motion in the right foot was limited to a moderate degree, and the patient found it difficult to move around except with the aid of a wheel chair. The rheumatologist thought the articular reaction was consistent with the changes which may accompany chronic ulcerative colitis and he felt that, in general, the patient's articular symptoms had improved since the onset of the articular difficulties. The left eye, with which the patient had had difficulty, was not congested. The visual acuity was 6/7 and there was a slight haze to the media noted on ophthalmoscopic examination. The pupil was dilated, probably as the result of the repeated instillations of scopolamine. On the basis of the patient's statements it seemed that she had recently experienced an inflammation of some part of the uveal tract. The sedimentation rate was 127 mm. per hour (Westergren method). The results of the remainder of the physical examination did not seem pertinent.

On April 29, five days after the administration of scopolamine was discontinued, the left eye again became red and the vision became blurred. A diagnosis of uveitis of the left eye was made. On May 2, a congestion of the left eye characteristic of episcleritis was superimposed on the circumcorneal flush which had been evident for the preceding three days. On May 4, a visual acuity of 6/20, with correction, was recorded. Slit lamp examination of the affected eye showed numerous pigmented cells moving in the aqueous current. No posterior synechias were visible but several pigmented precipitates on the posterior surface of the cornea could be seen. The congestion of the entire globe had become quite marked.

Injection of cortisone acetate was started on May 5. On the first two days a dosage of 200 mg. each was administered and 100 mg. each day thereafter, all injected by the intramuscular route. On May 10, the congestion of the left eyeball had disappeared and the pigment cells moving in the aqueous current had been reduced to about 10 cells per low-power field. The sedimentation rate was 118 mm. per hour. On May 15, the pigment cells had disappeared from the aqueous and injection of cortisone was discontinued. The sedimentation rate had dropped to 29 mm. per hour. The patient had received a total of 1.2 gm. of cortisone acetate over a ten-day period. The patient's difficulty with the right foot also had subsided. Although the daily number of stools had decreased while she was on cortisone therapy, the roentgenologic studies of the colon did not reveal any significant alteration of the inflammatory process as the result of administration of this hormone. The patient was dismissed on May 17.

About ten days after dismissal she noted a return of the congestion of the left eye. As the congestion became more pronounced, pain

ensued and finally the vision became misty. The patient had been taking aspirin for several days and a mydriatic had again been instilled, but she stated that this had had no noticeable effect on the ocular symptoms. She reported to us again on June 7.

Ophthalmic examination showed a marked congestion of the eyeball with the congestion most prominent surrounding a scleral nodule at the six o'clock meridian near the limbus. A pronounced "aqueous flare" and numerous pigment cells in the anterior chamber were visible with the slit lamp. Visual acuity of the affected eye was 6/60 with correction.

Instead of cortisone being given by intramuscular injection as on the previous admission, it was administered topically to the eye, 1 drop every hour, in the form of a suspension of cortisone acetate in a concentration of 8 mg. per cubic centimeter. The patient was maintained on this regimen of topical administration of cortisone for a period of twelve days. During this interval the "aqueous flare" and pigment cells in the anterior chamber disappeared and the congestion of the eye subsided except in the immediate vicinity of the scleral nodule. The elevation of the nodule had not been influenced by the topical administration of cortisone but the tenderness to palpation of the scleral nodule had improved.

It was thought necessary to readminister cortisone by the intramuscular route to bring about a resolution of the nodular scleritis. On June 19, 1950, daily injections of cortisone, 100 mg., were again started and the patient was given eleven injections (1.1 gm.). On this regimen the congestion and elevation of the scleral nodule subsided and the visual acuity improved to 6/12, with correction. The patient was again dismissed.

There had been no recurrence of the ocular disease three months after the last administration of cortisone according to word received from the patient.

This was the second of the 2 cases exhibiting the triad of colitis, arthritis and ocular disease, and the 2 cases were studied almost concurrently. In general the 2 patients showed a similar response to cortisone, but unlike the previous patient this individual experienced a recurrence of the scleritis when the cortisone had been withdrawn for a period of time.

This case was of particular interest in that it was one of the first in which cortisone was applied topically to the eye. When the hormone was first administered by this method we were skeptical that sufficient absorption of the suspended particles would occur to produce a significant effect. We were agreeably surprised at the beneficial effects on the eye that occurred within a period of twenty-four to forty-eight hours. The severity of the scleritis was such, however, that it was finally necessary to supplant the topical administration with systemic administration of the hormone. The cortisone eye drops were well tolerated by the patient.

Case 11.—A white man, aged 35 years, had been treated at the clinic on two past occasions for iritis of the right eye. His first attack of iritis had occurred during August 1947. Under the supervision of the Section on Ophthalmology the patient had received daily instillations of 10 per cent phenylephrine hydrochloride (neo-synephrine hydrochloride) and 1 per cent atropine in the right eye, intramuscular injections of omnadin and applications of hot fomentations to the right eye. Over a period of three and a half months of treatment this attack of iritis subsided without producing any impairment of vision.

The second attack of iritis had occurred in November 1948. Local, ambulatory treatment was carried out as with the previous attack, but in one week of treatment the right eye became worse and secondary glaucoma developed. The patient was then hospitalized for a period of ten days and the local treatment to the right eye was supplemented by five intravenous injections of triple typhoid vaccine. The glaucoma subsided and the eye improved, permitting the patient's release from the hospital. Ambulatory treatment was then recontinued for a period of another five weeks before the iritis subsided. Again no impairment of vision occurred.

On May 12, 1950, the patient returned, stating that the left eye had been red and painful during the preceding two days. A diagnosis of iritis of the left eye was made. The patient was sent for a general physical examination, but a clue to the origin of the iritis was not discovered. By the time this examination and all laboratory tests were completed, May 17, the left eye had become markedly congested, the aqueous was murky, with particles of exudate suspended in its dependent

portion, and the cornea showed a moderate degree of edema. The pupil had been kept reasonably well dilated by daily instillations of 1 per cent atropine. Posterior synechias were not present. Aside from a few pigmented cells the posterior surface of the cornea seemed free of precipitates.

Intramuscular injections of cortisone acetate were started on May 17. The first injection consisted of 200 mg., 100 mg. being injected daily thereafter. Atropine mydriasis was maintained. In five days the left eye showed definite objective evidence of improvement. On May 29, thirteen days after cortisone therapy was started, the left eye was white, the edema of the cornea had subsided, the murky appearance of the aqueous had disappeared and the exudate suspended in the aqueous had been absorbed. Because there were still a few pigmented cells moving in the currents of the aqueous, injection of cortisone was continued, but the patient received injections every other day instead of daily. On June 2, the injections of cortisone were discontinued, the patient having received a total of 1.6 gm. of the hormone.

On July 11, more than a month after injection of cortisone was discontinued, the patient returned for follow-up study. Visual acuity was noted to be 20/15 in each eye. There seemed to be no impairment of vision as the result of the third attack of iritis.

This case was of particular interest because we could compare the course and duration of iritis treated on two occasions by standard methods with an attack in which only cortisone was administered. In this regard the first two attacks served as a control against which the progress of the third attack could be evaluated. In each attack the visual acuity returned to normal after appropriate treatment, but in the attack wherein cortisone was administered the over-all period of disability was markedly shortened. The prompt response of the iritis to administration of cortisone in this case was similar to the response of the iritis associated with arthritis noted in case 1. Although a physical examination did not reveal a cause for the ophthalmic disease, it is possible that an arthritic diathesis will develop at some later date.

Case 12.—A white man, aged 43 years, had had rheumatoid spondylitis and recurrent uveitis of each eye for about twenty years. In 1946 iridectomy had been performed on the right eye because of secondary glaucoma. In general, this operation had been reasonably successful in maintaining the intraocular pressure of the right eye at a normal level. During January 1949, the patient had noted beginning loss of vision in each eye, and a diagnosis of complicated cataract of each eye was made. During July 1949 iridectomy preliminary to extraction of cataract was performed on the left eye. As the uveitis showed no tendency to flare following the iridectomy and remained quiescent for a period of six months, an intracapsular extraction of the complicated cataract was performed during December 1949. Although the operation for cataract was performed without complication, there was a severe exacerbation of the uveitis in the postoperative period. In spite of foreign therapy and local treatment to the left eye, a cyclitic membrane formed across the pupil and surgical coloboma of the iris, incorporating the iris tissue in its substance and fusing the iris to the anterior face of the vitreous. The visual gain as the result of the cataract extraction was nullified by this membrane. During March 1950 a secondary glaucoma was noted in the left eye.

When the patient reported to the clinic on May 22, 1950, a visual acuity of 6/120, each eye, was recorded. The intraocular pressure was 31 in the right eye and 41 in the left eye, Schiötz. A mature cataract was evident in the right eye. The edges of the surgical coloboma of the iris, right eye, were adherent to the capsule of the lens in many places. The superior pole of the cataract seemed fused to the posterior face of the right cornea by a broad synechia. In the left eye the iris was atrophic and the pupil was occluded. In neither eye did there seem to be any evidence of active uveitis.

On general physical examination active rheumatoid spondylitis was again noted with limitation of motion in the neck and back. The sedimentation rate was 54 mm. per hour (Westergren method).

With the idea of preventing or minimizing a postoperative uveitis we decided to administer cortisone prior to extraction of the cataract. On May 27, intramuscular injection of cortisone acetate, 100 mg. daily, was commenced. On June 2, seven days after injection of cortisone was started, an intracapsular extraction of the complicated cataract of the right eye was performed without difficulty.

During the first week of the postoperative period we noted some reactivation of the uveitis characterized by a mild circumcorneal flush and hazy media. Details of the fundus of the right eye, however, were visible. The uveitis continued to smolder in spite of the daily administration of cortisone and gradually adhesions formed between the surgical coloboma of the iris and the anterior face of the vitreous. The intraocular tension remained within the limits of normal.

On June 19, after the patient had received twenty-four injections (2.4 gm.) of cortisone the injections were given on alternate days. On July 1, after a total of 3 gm. of cortisone had been given, injection of the hormone was discontinued. Although the details of the fundus of the right eye were still visible, the media were becoming increasingly hazier and posterior synechias were more prominent. With a suitable correction for the aphakia the visual acuity of the right eye was improved to 6/60.

An attempt was made to carry on with administration of cortisone by the use of a suspension of cortisone applied topically. The diluent provided by Merck & Co. for investigation at this time proved too irritating to the eye and was discontinued after twenty-four hours' use.

This patient was the second on whom an intraocular surgical procedure was performed during the administration of cortisone. As with the other patient (case 7) the cortisone seemed to alter the expected postoperative course significantly in a beneficial manner. As compared to the stormy postoperative course of the left eye, the exacerbation of uveitis as the result of extraction of cataract from the right eye was very mild. However, it must be borne in mind that cortisone did not succeed in preventing an exacerbation but only minimized its severity. When the injection of cortisone was finally discontinued there was an increase in the signs of uveitis in the right eye, and when the patient was dismissed, eleven days after injection of cortisone was discontinued, it seemed likely that the pupil would be ultimately occluded, a fate previously experienced by the fellow eye, and the visual results of extraction of cataract would be nullified.

Case 13.—A white woman, aged 37 years, was sent to the clinic on June 2, 1950, because of unilateral uveitis that had been somewhat recalcitrant to therapy. She stated that about one month previously she had first noted onset of redness of the right eye. This symptom was followed in a few days by photosensitivity of the right eye and then pain and tenderness on motion of the eyeball or palpation of the eye. Four days after onset of these ocular difficulties, foreign protein and penicillin therapies were started. The patient received three intravenous injections of triple typhoid vaccine and two intramuscular injections of penicillin. In about one week on this therapy the eye seemed to improve but did not remain free of pain, redness or photosensitivity for more than three or four days.

Ophthalmic examination revealed a visual acuity of 6/60 in the affected right eye. The pupil had been widely dilated by a mydriatic. A moderate to marked degree of circumcorneal flush and scleral congestion was present. A marked "aqueous flare" with numerous cells in the anterior chamber was noted on slit lamp examination. A diagnosis of uveitis and scleritis of the right eye was made.

A physical examination and extensive laboratory studies were performed in a search for a possible cause of the ophthalmic disease. On dental examination deep caries with extensive periodontal destruction of one tooth was found. Inspection of the patient's throat revealed bilateral tags of tonsillar tissue that were considered by the otolaryngologist to be a possible focus of infection. Other than these findings the results of physical examination were normal and the laboratory tests were noncontributory to an etiologic diagnosis.

On June 3, administration of cortisone acetate as an aqueous suspension (8 mg. per cubic centimeter) was commenced. The patient was instructed to instill 1 drop of this suspension in the right eye every hour except during the period of sleep. After twenty-four hours of this treatment a definite decrease in the congestion of the eye had occurred. In three days the congestion had entirely subsided and the number of cells in the aqueous was much less than before. On June 12, after nine days of topical administration of this hormone, the cells in the anterior chamber had disappeared, the visual acuity had improved to 6/10, and the treatment was discontinued. No mydriatics were instilled in the right eye during the period of investigation

of the effects of cortisone.

On June 15, the patient underwent an extraction of the carious tooth, and on June 16, the tonsillar tags were extirpated. Neither of these surgical procedures caused any exacerbation of the ophthalmic disease.

The noteworthy feature of this case was the beneficial effect produced on this intraocular inflammation by the administration of cortisone only as a topical agent. This was the first case in which cortisone brought about an arrest of the inflammatory disease without being administered intramuscularly. It was estimated that this patient did not receive more than 8 to 10 mg. of the active hormonal agent per day on the surface of the eye. The response of the uveitis to such a small amount of cortisone was considered to be a remarkable circumstance.

Case 14.—A white man, aged 31 years, came to the clinic on June 12, 1950, because of redness, blurred vision and photosensitivity of the left eye of two weeks' duration. He stated that atropine had been instilled into the affected eye daily and frequent hot fomentations had been applied to the region of the left eye. He had received two intravenous injections of "typhoid" and one intramuscular injection of "milk." In spite of this treatment the left eye had become more painful and congested.

On ophthalmic examination a visual acuity of 6/100, left eye, was noted. A very marked congestion of the left eyeball was visible. Tonometric tension was within the limits of normal. On slit lamp examination of the left eye a mild degree of edema in the corneal substance was visible, a dense "aqueous flare" was evident, and a mass of fibrin could be seen in the dependent portion of the anterior chamber. No posterior synechias were visible. The posterior surface of the cornea was covered with tiny pigmented deposits. The pupil was regular and widely dilated. The results of ophthalmoscopic examination were not noteworthy except for the cloudy media. A diagnosis of anterior uveitis of the left eye was made.

Past history revealed two previous attacks of so-called iritis in the left eye during 1941 and 1946. Each of these attacks persisted one week with treatment.

A physical examination, blood studies and cutaneous tests were carried out in the search for a possible origin of the ocular disease. No cause was found. The sedimentation rate was 17 mm. per hour (Westergren method).

On June 12, intramuscular injection of cortisone acetate, 100 mg. each day, was started. The first definite evidence of objective improvement in the affected eye occurred on the third day after injection of cortisone was commenced. On the eighth day of treatment instillations of atropine into the left eye were stopped. On July 3, after the patient had received twenty-two injections (2.2 gm.) administration of cortisone was discontinued. The eye was completely free of congestion and photosensitivity, the aqueous had cleared, and the pupil had returned to its usual diameter. The tiny pigmented deposits on the posterior surface of the cornea remained and were probably responsible for the incomplete return of vision to 6/15.

This patient was considered to have very severe anterior uveitis before administration of cortisone was started, and it was not until two days had passed that any noticeable effects of the cortisone were observed. The over-all treatment period of twenty-two days was somewhat longer than in similar cases in which the anterior uveitis was not associated with arthritis.

Case 15.—A white man, aged 37 years, reported to the clinic on June 24, 1950, because of congested, irritable eyes that had seemed moderately sensitive to light for a period of one month. Previous treatment had consisted of various "eye drops" on the assumption that the patient was suffering from conjunctivitis.

On ophthalmic examination a diffuse congestion of moderate degree was present in each eye. Closer inspection of each eyeball revealed that the congestion had a slight violaceous hue. Each globe was slightly tender to palpation. A mild edema in the periphery of each cornea was noticeable on study of the anterior segments of the eyes with the slit lamp. Vision was 20/20, each eye. A diagnosis of bilateral scleritis was made.

On June 30, a solution of cortisone hemisuccinate (10 mg. per cubic centimeter) was applied to the eyes, 1 drop each hour. On the following day we noted the congestion of each eye to be about 40 per cent less. The topical

administration of cortisone was continued, but no further evidence of improvement in the ocular disease occurred.

On July 5, the topical administration of cortisone was discontinued and the daily intramuscular injection of 100 mg. of cortisone acetate was started. On the day following the initial injection of cortisone the photosensitivity subsided. After seventeen injections (1.7 gm.) the congestion of each eye had subsided, the eyes felt normal, and the tenderness had disappeared. The injections of cortisone were discontinued. During the period when the patient was receiving cortisone he noted a gain of 9 pounds (about 4.1 kg.).

Ten days after the injection of cortisone was discontinued the patient noted a recurrence of the congestion and photosensitivity, and on the thirteenth day, August 2, a second series of daily intramuscular injections (100 mg.) of cortisone was commenced. The eyes again responded to this hormone, but eleven injections (1.1 gm.) were necessary to rid the eyes of their scleritis.

The patient was then symptom-free for a period of seven days, only to note again a return of the congestion of each eye. An ointment containing cortisone 21-hemisuccinate (25 mg. per gram of base) was then applied to each eye four times a day. In a period of three days the congestion of each eye had again subsided. This patient has now gone one month without noting a recurrence of ocular symptoms.

This case of scleritis was very similar to case 2 in its behavior to administration of cortisone, in that suppression of the symptoms could be brought about by this hormone, but relapses occurred when cortisone was withdrawn. Here again, cortisone probably did not shorten the over-all duration of the disease (three months) but forestalled possible complications of the prolonged scleritis.

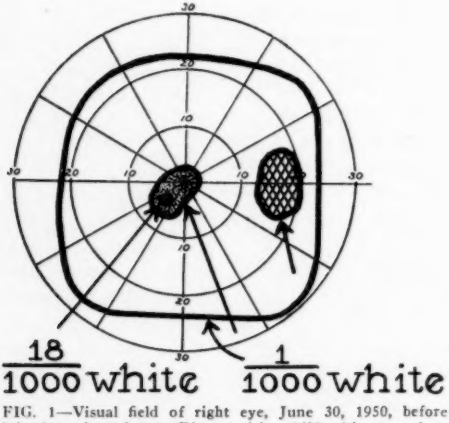

FIG. 1—Visual field of right eye, June 30, 1950, before injection of cortisone. Distant vision 6/30 with correction; near vision 14/21 with correction.

Of all the ocular disorders studied in this investigation scleritis seemed to respond more promptly to either topical or parenteral administration of cortisone than any of the other inflammatory conditions of the eyes.

Case 16.—A white woman, aged 27 years, came to the clinic on June 29, 1950, because of blurred vision of the right eye of two weeks' duration. On ophthalmic examination a visual acuity of 6/30, right eye, and 6/10, left eye, each with correction, was noted. The patient was unable to read the finest print on the American Medical Association reading card with the right eye, although she was able to do so with the left eye. A yellowish, slightly elevated (less than 1 diopter) area of exudate at the right macula measuring 3/4 disc diameter in size was noted on ophthalmoscopic examination. Visual field studies showed a para-

central scotoma in the right visual field (fig. 1). A diagnosis of acute choroiditis of the right eye was made.

Physical examination did not reveal any clue as to the origin of the ocular difficulty.

On June 30 daily intramuscular injection (100 mg.) of cortisone was commenced. By July 5, six days later, it was evident that the choroiditis was healing. Thirteen injections (1.3 gm.) of cortisone were administered to the patient. When injection of the hormone was stopped a sharp and distinct foveal reflex was once again visible adjacent to an area of residual edema. With the right eye the patient could read the finest print on the American Medical Association reading card and the distant visual acuity had improved to 6/12. Only a tiny residual scotoma adjacent to the fixation point was noted on visual field study (fig. 2).

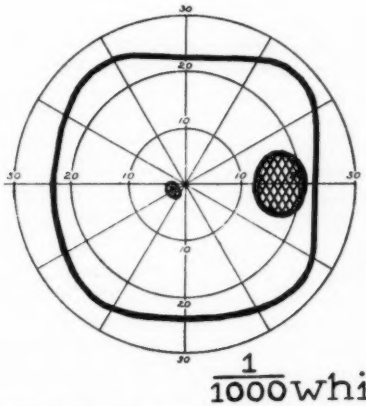

FIG. 2—Visual field of right eye, July 14, 1950, after injection of cortisone. Distant vision 6/12 with correction; near vision 14/14 with correction.

In contrast to case 8, in which central choroiditis was also present, the choroiditis in this case seemed definitely improved by the administration of cortisone. It is possible that the duration of the inflammatory lesions before cortisone was administered in the respective cases was the determining factor in the contrasting response to cortisone. In one case the lesion had existed for three months prior to study; in the other, two weeks. It seemed to us that the healing of the choroiditis in the latter case was more rapid with cortisone than would have occurred had the hormone not been given.

COMMENT

From our observations as to the effect of cortisone on cases of anterior uveitis, posterior uveitis, scleritis, keratitis, choroiditis, and vernal conjunctivitis it is evident that this hormone of the adrenal cortex can exert a profound influence on some types of ocular disease. In those cases wherein this hormone exerted a beneficial effect its action was more prompt than had been noted with other therapeutic measures that had been tried prior to administration of cortisone. This was particularly true among those cases in which foreign protein treatments had been given previously to control the ocular disease. The absence of chills and fever and the general feeling of "well-being" when cortisone was administered made this hormone more desirable than foreign protein therapy to patients who had ex-

perienced both forms of treatment. This feature was particularly attractive in the management of ocular disease among people more than 60 years of age, to whom foreign protein therapy might be hazardous. Not only its potency, but its convenience of administration from the patient's standpoint, then, should make it a desirable agent for future therapeutic trial in many types of ocular disease.

Although in the majority of our cases this hormone produced a suppression of the disease process, in some cases (cases 3 and 8) cortisone seemed to be without effect. It is our impression that cortisone will prove to be most effective in those ocular diseases of short duration and in those which have an acute rather than a chronic course. It is probable that an irreversible stage is reached by many chronic ocular diseases and when this comes about cortisone will be of little benefit.

Among the cases of acute ocular disease of short duration which showed a beneficial response to cortisone it was not possible to predict, prior to the administration of this hormone, how promptly the disease would respond. Even in the same patient to whom cortisone was administered at various times because of a recurrence of symptoms the response of the disease process was variable. It was not understood why the ocular disease of a given patient reacted differently to the administration of cortisone on two different occasions nor why the hormone varied in its effectiveness among patients who exhibited very similar types of ocular disease.

A prominent feature among the majority of cases under investigation was the tendency for the disease process to recur or to produce symptoms again when cortisone was withdrawn. This was particularly noticeable among the diseases of the eye associated with arthritis. A tendency to relapse was so common that it would be in error to consider that a cure had been effected by cortisone alone. In several cases the suppression of symptoms both subjectively and objectively during administration of cortisone was so complete that by former standards of clinical progress the disease process should have been cured, only to flare to its precortisone intensity when the administration of this hormone was stopped. This behavior would indicate that the hormone does not eradicate the etiologic agent or causative irritant. In those cases in which such a recurrence was noted, the relapse usually occurred in from five to seven days. In an attempt to circumvent this problem of relapse several methods of withdrawing the hormone were tried, but none of them proved definitely successful. Among the cases in which the ocular disorder seemed allied to an arthritic diathesis the articular difficulties showed a more prompt response to the administration of cortisone than the disease of the eyes, but the articular symptoms recurred more promptly and more frequently than the ocular symptoms when administration of cortisone was stopped.

In our administration of cortisone by the intramuscular route we came to favor a dosage schedule of 100 mg. daily. The effect of an initial dose of 200 mg. did not seem sufficiently prompter to warrant the increased quantity of hormone. It was our impression that on a schedule of 100 mg. daily an effect in any ocular disease responsive to cortisone can be expected in from ten to fourteen days. We did not feel it worth while to continue administration of the hormone beyond a two-week period if no objective improvement was visible.

Among those cases in which the hormone proves to be of benefit the question arises as to how much cortisone can be given with safety. It was our impression that on the basis of an injection of

100 mg. daily, thirty injections or 3 gm. can be given with reasonable safety, although from 2 to 2.5 gm. (twenty to twenty-five injections) will usually suffice. In case 6, in which the patient was an 8-year-old boy, 7.47 gm. of cortisone was administered by means of 113 injections over a period of 146 days, and in case 7, in which the patient was a 54-year-old woman, 6.6 gm. of cortisone was administered by means of 74 injections over a period of ninety-three days. These patients were considered to present exceptional problems warranting a prolonged use of cortisone. In one of them signs of intolerance developed. No permanent ill effects as the result of prolonged administration of cortisone seem to have developed in follow-up periods of two and a half and three months, respectively. If dosage beyond 2.5 gm. is to be given, due consideration should be given to the mental and physical "let down" which usually occurs when the hormone is withdrawn.

As suspensions and solutions of cortisone for topical administration become commercially available it will be possible to replace or supplement the intramuscular injections. We have not found it possible to predict which cases will respond to topical administration alone and in which cases it will be necessary to give the hormone by the intramuscular route to bring about a desired effect. It seems feasible to prescribe cortisone drops or ointment for the ophthalmic disorder during the period immediately following the withdrawal of cortisone systemically. A recurrence of ocular symptoms might then be minimized.

In our opinion the future use of cortisone among cases of smoldering or active uveitis requiring intraocular surgical procedures is an exciting probability. In the limited sphere in which we have studied this combined use of the hormone with intraocular surgical procedures it has seemed particularly effective in helping to control glaucoma secondary to uveitis. In the surgical cases among which it has been employed the glaucoma had proved recalcitrant to nonsurgical measures. Although we had hoped the visual result would be better as the consequences of extraction of cataract in case 12 and the uveitis would be completely arrested, our experience with the administration of cortisone in this case proved that major intraocular surgical procedures could be carried out without fear of marked exacerbation of the uveitis during the immediate postoperative period.

It does not seem amiss to speculate on the possible usefulness of cortisone among ocular diseases other than those recorded here. In the uveitis following extraction of cataract, in sympathetic ophthalmitis, in keratoconjunctivitis sicca, in optic neuritis, and among cases of retinal periphlebitis of obscure origin cortisone might prove of value. In 1 case of acne rosacea keratitis investigated by one of our colleagues, Dr. H. L. Bair, cortisone seems to be having a beneficial effect. The future of research in the field of ocular disease as concerns the effects of cortisone still beckons with some exciting possibilities.

In the last analysis there is much to be learned about the hormones of the adrenal cortex, and the action of cortisone itself on disease processes in the eye is still an enigma. Our knowledge, to date, of this action might best be summarized in the words of Hench:

> Cortisone appears to have little or no effect on the irritant but seems to provide the susceptible tissues with a shield-like buffer against the irritant . . . it does not of itself put out the fire (remove the irritant) nor does it serve as a carpenter to repair the fire's damage. In short, cortisone exerts its dominant influence on the pathologic physiology (the disease itself) rather than on the pathologic anatomy (the residues) or on the etiologic factor of these conditions.

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CLINICAL EXPERIENCES WITH ACTH AND CORTISONE IN OCULAR DISEASES

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THIS paper is a report of the results of adrenocorticotropic hormone (ACTH)* and 17-hydroxy-11-dehydrocorticosterone (cortisone)† therapy in a variety of eye diseases. Because of the limitations of time it must be given in rather summary fashion.

METHODS OF TREATMENT

For *parenteral therapy* all patients were hospitalized and studied for evidence of contraindications, including diabetes, cardiovascular disease, hypertension, and renal disease. Those that were considered good risks were then started on intramuscular injections every six hours and the dosage varied according to the suppression of circulating eosinophils. This index appeared to be prompt and reliable with ACTH, somewhat slower and more erratic with cortisone. Initial dosage for ACTH was 20 to 30 mg. every six hours; for cortisone, 25 to 50 mg. It is possible that lower dosages might have been as effective in some cases.

Throughout treatment, a constant watch was maintained for evidences of glycosuria, hyperglycemia, hypertension, fluid retention, cardiac changes, kidney damage and mental depression, which were taken as indications for withdrawal of treatment. In general, the patients were carried on the amount of hormone necessary to maintain an eosinophil drop of over 50 per cent until the disease process was controlled. Then various methods of "tapering-off" were used to avoid the relapse liable to occur with abrupt termination.

Local treatment was confined to cortisone, for it would be unreasonable to expect ACTH to act directly on the eye (local ACTH was actually used in a few eyes to prove this point and did prove ineffective and somewhat irritating). Most of the local treatment consisted of hourly or bihoral instillations of a drop of saline suspension of cortisone acetate. After some experimentation, it appeared that the optimal dilution was in the range of 10 to 20 per cent of the standard cortisone preparation, or between 2.5 and 5.0 mg. per cubic centimeter. Some cases were treated by subconjunctival injections, for which

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*The ACTH used in this study was obtained through the courtesy of Dr. John R. Mote of Armour Research Laboratories.

†The cortisone (cortone acetate) was obtained through the courtesy of Dr. J. M. Carlisle of Merck Laboratories.

the most efficient dosage seemed to be about 1 cc. (25 mg.) undiluted cortisone twice a week.

COMPLICATIONS

It is to be emphasized that these agents are powerful and not to be administered lightly. In spite of rather rigid criteria for selection of patients and in spite of careful control, complications—both systemic and ocular—were encountered. There were no systemic complications with local cortisone treatment. The commonest change noted was the appearance of "moon facies" as seen in early Cushing's syndrome. This, however, was not serious and tended to regress on withdrawal of the drug. The next commonest side effect was a change in mood. Nearly half of our cases developed a feeling of well-being or elation bordering on euphoria and a few of them became temporarily depressed on cessation of treatment. A few became depressed and dejected under therapy and one had an overt psychotic reaction with attempted suicide. She required months of psychiatric hospitalization. The third commonest complication was fluid retention with a gain in weight and disturbance of electrolyte pattern. Others included hypertension, hyperglycemia with glycosuria and one minor-branch coronary occlusion which may or may not have been related to the treatment.

Ocular complications were confined to alterations in intraocular pressure and one case of what appeared to be local sensitization to cortisone drops. These will be dealt with subsequently.

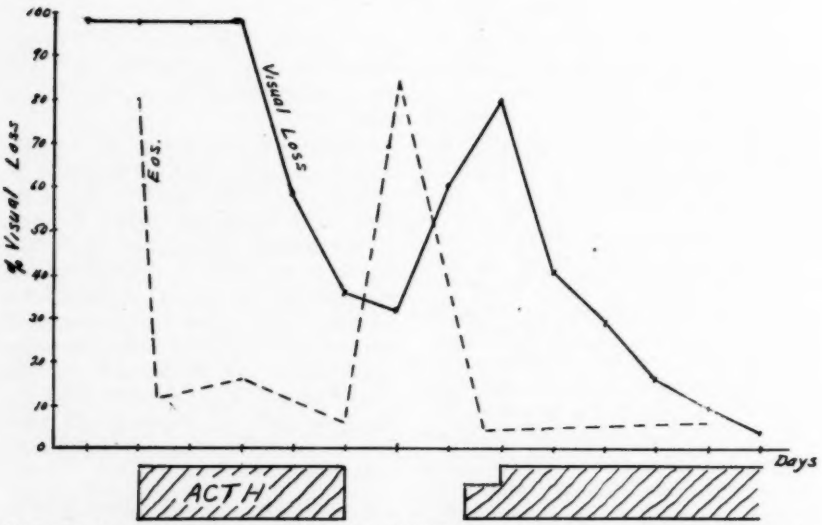

FIG. 1—Optic neuritis tested for specific effect of ACTH by withdrawal and resumption of treatment.

EVALUATION

Evaluation of results is not entirely simple. Subjective tests must be accepted with caution because of the enthusiasm of many patients for a new drug and the euphoric reaction of patients to these agents. In addition, we have noted an apparent tendency towards increased perceptive ability in normal eyes. One extreme example is a young adult whose

corrected visual acuity in his normal eye rose from 20/20 to 20/15 to 20/12 to 20/10 while receiving intramuscular ACTH for choroiditis in the opposite eye! Therefore, as far as possible, results have been graded on objective observations including aqueous flare, keratic precipitates, anterior chamber cell count *in vivo*, vitreous turbidity, redness, discharge, tissue changes in cornea, iris, choroid and retina, elevation of optic disc, and tonometric measurements. Another difficulty arises in assessing effect in acute processes subject to natural remissions. The method of gauging these effects is shown in figure 1, a case of acute retrobulbar neuritis in which ACTH was given with a prompt eosinophil drop, resolution of scotoma, and improvement in acuity. As visual loss decreased, a placebo was substituted with a prompt rise in eosinophil count and recurrence of visual loss. On resumption of ACTH, improvement was resumed and it was maintained as the drug was slowly withdrawn when improvement was complete. We feel that this type of evidence is strongly suggestive of a drug-induced result and not coincident natural remission.

RESULTS

Eliminating those cases in which there is not yet adequate follow-up, we have to analyze 75 cases treated by intramuscular ACTH, 34 cases by intramuscular cortisone, 8 cases by a combination of the two, 139 cases by topical cortisone, and 59 cases by subconjunctival and topical cortisone. Many forms of "tapering-off" have been tried in an effort to minimize relapses, but this phase is still under study. Except where otherwise stated, the therapeutic effects of intramuscular ACTH or cortisone or both will be grouped together since we have not been able to discern significant differences.

Iridocyclitis was treated parenterally in 13 cases (table I). Prompt and complete arrest of the disease in 10 cases out of 13 (all severe) far exceeds results from any previous form of therapy. One of the 3 failures did not show an appreciable eosinopenia, indicating poor systemic response of the individual to the agent. This same patient later responded to induced fever treatment, as did one other failure. He and another failure developed marked secondary glaucoma, as did one successful one which was carried through on paracenteses. Three of the successful cases developed relapses, each of which responded to repetition of treatment.

TABLE I

IRIDOCYCLITIS

	NO. CASES TREATED	IMPROVED	RELAPSE	FAILURE	POOR EOSINOPHIL RESPONSE	GLAUCOMA	IMPROVED WITH FEVER
Granulomatous	5	3	1	2	1	2	1
Nongranulomatous	4	3	1	1	0	0	1
Tuberculous	2	2	0	0	0	0	–
Sarcoid	2	2	1	0	0	1	–
Totals	13	10	3	3	1	3	2

Local cortisone in the subconjunctival or topical form has been used in 22 cases of iridocyclitis (not all severe). By these methods longer, safer, and ambulatory treatment can be had. There was only one failure, one severe secondary glaucoma, and four relapses. All relapses re-

TABLE II

UVEITIS

	NO. CASES TREATED	IMPROVED	RELAPSE	FAILURE	POOR EOSINOPHIL RESPONSE	GLAUCOMA	IMPROVED WITH FEVER
Granulomatous	9	6	2	3	1	2	1
Nongranulomatous	7	5	1	2	2	2	–
Tuberculous	4	3	1	1	1	0	–
Totals	20	14	4	6	4	4	1

sponded promptly to resumption of treatment. One of these cases was one of the failures on 100 mg. of ACTH a day; the patient had developed secondary glaucoma on intramuscular treatment and had been refractory to induced fever. This patient did not develop glaucoma on the subconjunctival regime.

Generalized uveitis was treated intramuscularly in 20 cases (table II). Of 14 successful cases, 4 later relapsed but all 4 responded to further treatment. Of the 6 failures, 3 were associated with failure in eosinophil suppression and 4 developed secondary glaucoma. One improved later with intravenous typhoid vaccine.

Only 5 cases of mild generalized uveitis were treated locally. All did well.

Sympathetic ophthalmia is considered apart from other cases of uveitis because of its importance as an essentially incurable disease. Five cases were treated (table III). In 4, diagnosis was confirmed histologically in the enucleated inciting eye. In the other case, enucleation was not done. A flare-up of the disease in a case of eighteen years duration was subjectively improved but showed no objective signs better than might normally be expected in such an episode and is classed as unimproved. A flare-up in a case of six years standing responded dramatically to local treatment and has not relapsed since. An

TABLE III

SYMPATHETIC OPHTHALMIA

DURATION	HISTOLOGICALLY CONFIRMED	DOSE (mg.)	RESULT	RELAPSE
18 years	Yes	ACTH, 2030	No improvement	——
6 years	Yes	Subconjunctival cortisone, 2 weeks Topical cortisone, 6 weeks	Improvement	None, 6 months
6 months*	Yes	ACTH, 3160 Subconjunctival cortisone, 2 weeks	No improvement	——
15 days	Yes	ACTH, 2430 Topical cortisone	Arrest	None (topical cortisone continued)
14 days	No	ACTH, 1680 Cortisone, 1620	Arrest	None, 5 months

*Secondary glaucoma requiring paracenteses.

active six-months-old case responded only by going into severe secondary glaucoma requiring multiple paracenteses for control. Two fresh cases responded dramatically and with the aid of topical cortisone have maintained 20/20 and 20/40 vision, respectively, without inflammatory relapse. In the last of these, an intradermal uveal pigment skin test was injected on the fifth day of intramuscular ACTH. Histopathologic examination showed less reaction than is seen in many "negative" tests (fig. 2). This incidental finding leaves room for more speculation on the nature of the disease as well as the nature of the therapeutic effect.

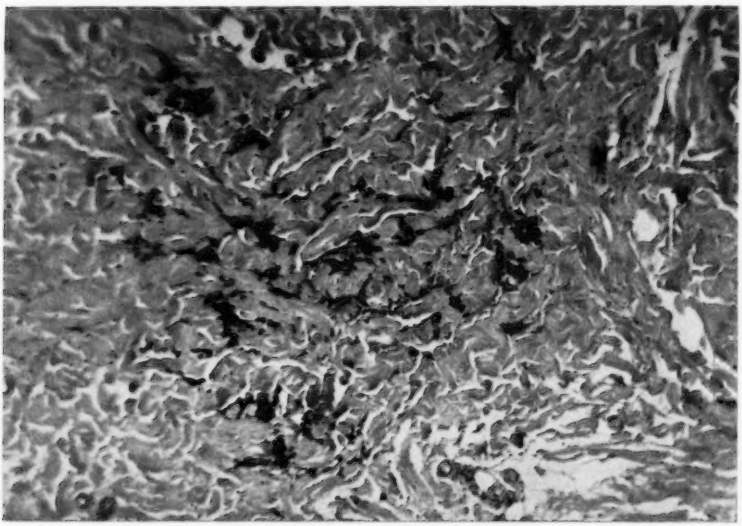

FIG. 2—Uveal pigment skin test under ACTH therapy.

Choroiditis was treated systemically in 11 severe cases. Eight cleared promptly, with 1 relapse that responded to local treatment and 3 failures. One failure was the patient whose treatment had to be stopped because of acute psychosis and one failed to give a satisfactory eosinophil response in spite of large dosage. Twelve less severe cases were treated subconjunctivally and topically with slow but satisfactory improvement in all twelve.

Glaucoma has been somewhat of a problem in our series of patients in contrast to the findings of Blake and his coworkers.[1] In 6 cases of secondary glaucoma the tension responded in 2, was unaffected in 1, and rose seriously in 3. As mentioned above, secondary glaucoma was precipitated in 4 out of 20 cases of uveitis and in 3 out of 13 cases of iridocyclitis while under systemic treatment. Five of these cases were treated with ACTH, 2 with cortisone. One case out of a total of 27 treated with local cortisone developed severe secondary glaucoma. No cases of secondary glaucoma have yet been treated locally.

Of the 8 cases of secondary glaucoma precipitated during treatment, 4 required emergency surgery for control.

Cataract is a condition in which improvement would not be expected. However, one patient, the wife of a physician, was treated for eleven days with 1250 mg. of ACTH for immature senile cataracts. This was done only at the virtual demand of the patient and her husband who was a professor on the faculty of another medical college. There was complete eosinopenia but no detectable change in the eyes, and the only result was transient uterine bleeding many years after the menopause.

In addition, we have observed cataracts of various types and stages both in patients elsewhere in this series and in patients not in this series who were being treated in other departments of the hospital for various diseases. There has been no change of any type in any of these 51 cataracts.

Optic neuritis in the visible and in the retrobulbar forms was treated parenterally in 4 cases and subconjunctivally in 4 cases. One retrobulbar neuritis had a definite, and another a probable, diagnosis of multiple sclerosis. Both of them returned to normal promptly on systemic ACTH. One visible bilateral optic neuritis improved and one failed. Two of those treated subconjunctivally improved; two failed. It is to be noted that the failures did not improve with other types of treatment.

Retinitis pigmentosa has been treated systemically in 10 cases and locally in 58 cases. Some of the systemic cases have had more than one course and some of the local cases have had prolonged treatment. In none has there been a sudden or dramatic change. However, in some of the early cases there has been enough indication of more than chance improvement in vision, fields, and dark adaptation to warrant further study of these patients. The results are similar to those of the Ford Hospital group.[8]

Corneal disease would appear to be an ideal site for local therapy. Forty cases were so treated. In addition, 4 cases were treated systemically. Systemic treatment failed in 1 case of Fuch's dystrophy, 1 hypopyon ulcer, 1 syphilitic interstitial keratitis and 1 syphilitic keratitis profunda.

Local treatment resulted in prompt clearing in 1 dendritic ulcer, 1 filamentary keratitis, 1 acute phlyctenular keratitis, 2 recurrent erosions and 5 superficial ulcers. Ten Fuchs' dystrophies appeared to be improved but did not hold and the end result was no improvement. Similarly, 5 out of 7 cases of bullous keratitis seemed to show temporary improvement which did not persist. In contrast to the case treated systemically, 5 cases of interstitial keratitis (including the systemic failure) responded well to local treatment with rapid regression of the inflammatory activity and decrease in vascularization. Two cases of superficial punctate keratitis remain well on drops but recur on omission. Six cases of unclassified keratitis had indifferent results but all had relief of pain.

Retrolental fibroplasia has been said to respond to ACTH through its inhibition of fibroplastic processes.[2,9] Our experience in 5 cases has not been encouraging. Two well-developed cases on 25 mg. ACTH per day were utterly unaffected. Of 3 early cases similarly treated, 1 was unaffected, 2 appeared to regress, but after withdrawal 1 of these went on to develop the disease.

Severe *diabetic retinopathy* was treated with local cortisone in 28 cases without significant improvement.

Central serous retinopathy was treated subconjunctivally in 3 cases with prompt and complete recovery.

External allergic reactions were treated with cortisone drops in 4 cases.

Two cases of drug sensitivity cleared promptly. One case of vernal catarrh improved markedly and one barely at all. One patient who was receiving cortisone drops for corneal vascularization developed a marked local sensitivity reaction which subsided on withdrawal of cortisone.

Conjunctivitis was treated in 8 cases. Three cases of epidemic keratoconjunctivitis and 2 cases of angular conjunctivitis responded dramatically to cortisone drops and cleared in twenty-four hours. Three cases of chronic blepharoconjunctivitis did not respond.

Episcleritis responded promptly to local cortisone in 4 cases.

Of 9 cases of *macular degeneration* of the disciform type, 6 were unaffected, 2 showed questionable, and 1 definite but slight, transient improvement.

No significant improvement was found in 3 cases of optic atrophy, 2 cases of Eales' disease, or 3 cases of choroideremia.

COMMENT

As a result of these studies and recent reports in the literature,[3,4,5,6,7,11,12] one definite conclusion can be drawn. These new agents, adrenocorticotropic hormone and 17-hydroxy-11-dehydrocorticosterone are producing startling results in eye disease. Conclusions on methods of action would be a little premature. When we were using only systemic treatment, we were inclined to liken the effect to that of foreign protein shock treatment of an unusually efficient character. This idea was in harmony with Selye's theories.[10] The striking effect of local cortisone somewhat upsets this train of thought. Certainly these drugs do suppress inflammatory processes, but whether they do so by antihistaminic, anti-infectious, cyto-depressant or some other action remains to be determined.

The relative merits of systemic ACTH and systemic cortisone are hard to assess. It is our impression, although we cannot document it statistically, that in severe disease ACTH is rather more effective. At the same time, we have had more complications with ACTH, which we ascribe to its wider hormonal activity. This we feel is particularly to be noted in regard to its water-binding activity and secondary glaucoma.

Experience with subconjunctival and topical cortisone has been very encouraging. It would appear that the use of cortisone in the form of drops is fairly efficient for disease of the anterior segment and that enough absorption takes place from subconjunctival injection to affect the posterior portion of the globe. The amount of material used locally is far too small to assume that this could be a portal of entry for systemic effect. The failure of local ACTH tends to confirm this. If we compare the weight of the eye with total body weight, it represents only about 1/100 of 1 per cent. Assuming that most of the drug applied locally acts locally in the eye, a subconjunctival dose of cortisone of 25 mg. every three days should make available for ocular use six or seven hundred times as much as three days of 100 mg. per day distributed evenly throughout the body. Granted that this comparison may be rather erratic, it still indicates that local use is probably an efficient means of getting the desired effect on the eye. The good results of local treatment tend to confirm this notion. Furthermore, the unilateral response to unilateral cortisone in a few cases of bilateral disease argues strongly for simple local effect.

Our present concept of treatment of choice is the use of cortisone drops about hourly while awake and every two hours during sleep for anterior ocular disease, subconjunctival cortisone for deeper ocular involvement, and intra-

muscular ACTH in resistant or very severe cases. Regardless of form of treatment, gradual withdrawal is important. At present, the best method seems to be gradually decreasing doses of topical cortisone. Study has just been begun on a long-acting form of ACTH. The use of this preparation and the local use of water-soluble forms of cortisone will have to wait a later report.

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DISCUSSION

SOL ROME, M.D., Los Angeles, Calif.: I appreciate the privilege of speaking to you on the subconjunctival injection of cortisone in inflammatory eye conditions. I wish to thank both Dr. Benedict and Dr. Reese for the opportunity of adding our results to the carefully worked out studies of Dr. Henderson and Dr. McLean, and their respective groups. They are both to be congratulated on being among the first to see the possibilities in the application of these hormones to ophthalmology.

Dr. Raphael Koff and I have been investigating the effect of cortisone and ACTH at the Los Angeles County General Hospital since November 1949. In April 1950 we began using cortisone subconjunctivally after careful animal experiments proved its harmlessness. We have become so impressed with its effectiveness when used subconjunctivally that we now use this method routinely in anterior segment ocular conditions in preference to systemic administration.

The following advantages of this method of administration as compared with systemic ACTH and cortisone have been noted:

1. No side effects, local or systemic, have been observed in 108 cases in which cortisone was injected subconjunctivally.
2. No immediate or late harmful sequelae, either local or systemic, have occurred in any of these cases.
3. There is no need for hospitalization or laboratory follow-up.
4. Only small amounts of the drug are used.
5. It is as effective as systemic administration in anterior segment lesions.
6. The hormone under the conjunctiva has a repository effect so that a single dose maintains its effect for ten to fourteen days.
7. Its effect becomes evident more rapidly.

The method of administration is as follows: 0.4 to 0.6 cc. of cortone (Merck) undiluted is injected under the conjunctiva 5 to 6 mm. above the upper limbus with a 23- to 25-gauge needle. The eye is first anesthetized with pontocaine and a pledget of 10 per cent cocaine is placed at the site of the injection. The procedure is practically painless. The small amount of discomfort for the next six to twelve hours is easily controlled by codeine. Subsequent injections, when indicated, are given at different sites. This deposit of cortisone under the conjunctiva disappears gradually within eight to twelve days. During the time that it is being absorbed, it appears to be continuously exerting its effect.

The subconjunctival injection of cortisone in acute iritis, in various forms of keratitis, and in vernal catarrh parallels that of systemic ACTH or cortisone. Its effect, however, becomes evident more rapidly, within six to twelve hours.

In chronic uveitis, subconjunctival cortisone acts like ACTH. It produces a remission in about 50 per cent of the cases. With subsequent injections, the duration of these remissions becomes progressively longer. We have also been able to control the relapse on withdrawal of ACTH therapy with subconjunctival cortisone.

Twelve cases of acute and acute recurrent iritis are presented. These cases are being presented because they had received the usual treatment, including local atropine, intravenous typhoid, and salicylates without improvement. In 10 of these 12 cases subconjunctival injection of cortisone produced remarkable improvement within forty-eight hours. Pain, which in some of these cases was intense, disappeared in four to twelve hours. Hyperemia of the bulb was markedly decreased. Solid gelatinous exudate, where present, melted away in twenty-four hours. Newly formed iris adhesions, previously unresponsive to any type of mydriasis, were broken away and the pupil became widely dilated.

In 2 of these patients with bilateral iritis, cortisone was injected subconjunctivally into the worse eye. In each case the eye that was given the cortisone improved rapidly while the other remained stationary or deteriorated. In a case of iritis combined with secondary glaucoma, cortisone apparently prevented the flareup of iritis after surgical intervention which would ordinarily have been expected.

Seven cases of various types of keratitis are presented. These also are being shown because they had all proved refractory to other

methods of treatment, some for years. One case (recurrent erosion) failed to respond. In the others, pain and photophobia ceased within forty-eight to seventy-two hours. Redness of the bulb disappeared uniformly. Gross vascularization was markedly decreased. Superficial corneal conditions such as vesicles, filaments, active infiltrates and edema began to clear within forty-eight hours. The slit lamp showed a very noticeable diminution in the number and size of vessels carrying circulating blood. These 6 responsive cases are:

1. Filamentary keratitis
2. Vesicular keratitis
3. Sjogren's syndrome
4. Sclerosing keratitis
5. Interstitial tuberculous keratitis
6. Acne rosacea keratitis

Just as Dr. Henderson and Dr. McLean have found, our results also indicate that the best response in uveitis may be expected when these hormones are applied in acute processes. We may anticipate that one of the principal fields of usefulness of these hormones will lie in preventing these acute processes from becoming chronic. Hormone therapy should be instituted early, before irreversible changes take place.

On the basis of over one hundred cases with not one untoward or harmful result, it is felt that the subconjunctival injection of cortisone is a safe and very useful procedure. It has all the advantages over the older forms of therapy, such as typhoid, which Dr. Henderson and Dr. McLean have shown for systemic cortisone and ACTH, with none of the disadvantages or side effects of this systemic administration.

FREDERICK C. BLODI, M.D., New York, N. Y.: I should like to add a few words on the use of ACTH during the acute stages of retrolental fibroplasia. Together with the pediatricians, Dr. W. A. Silverman and Dr. R. L. Day, we began the trial of this new drug at the Presbyterian Hospital after discouraging results with vitamin E. In addition to 86 patients treated with ACTH or cortisone, out of which 49 were treated locally, at the Eye Institute, we have so far treated 14 infants affected with retrolental fibroplasia at Babies Hospital. The results are such that we have been encouraged to continue the use of the drug on an experimental basis. The series is still too small to justify either a definitive statement of the action of the drug in this condition or a recommendation for the drug except where controlled observations can be carried out.

The rationale for the use of ACTH in retrolental fibroplasia is as follows:

1. We have good clinical and histologic evidence that retrolental fibroplasia is primarily a disease of the blood vessels characterized by a dilatation of the existing blood channels and by their proliferation into the vitreous. It is known that induced hyperadrenocorticism inhibits the growth of mesenchymal cells, and it could be shown that cortisone specifically inhibits the growth of capillaries. It should be reasonable to expect that ACTH will halt the vascular overgrowth which marks the beginning of retrolental fibroplasia.

2. In addition to this pharmacologic effect, there is room for speculation that there may also be a physiologic basis for using ACTH in these premature children. We have ample evidence that there is a hyperadrenalism during the last trimester of pregnancy caused by the probable formation of ACTH and adrenal cortical steroids in the placenta. These hormones may conceivably be necessary for the normal development of the fetus. Premature separation from the maternal hormonal environment may have a deleterious effect.

3. Furthermore, we know that retrolental fibroplasia is a self-limited disease. We have never seen it develop in an infant older than 3 months. We have to carry the child only over this dangerous period and the duration of induced hyperadrenocorticalism can be comparatively short.

Our indication for starting the administration of ACTH lies in the ophthalmoscopic picture. Only when signs of definite and rapid progression, such as retinal edema or retinal detachment, appear do we begin treatment. Dilatation and tortuosity of the retinal vessels with fundus hemorrhages are not an indication for starting ACTH. We know too well that the percentage of spontaneous regression is high in this stage of the disease.

We usually give 20 to 25 mg. of ACTH each day for 14 days. A second course can be given if the disease becomes reactivated after cessation of treatment, an eventuality that has arisen in 2 of our cases.

The side effects of ACTH, all apparently temporary, consist of cessation of growth, tachycardia and glycosuria. Electrolyte imbalance has not proved troublesome, and we do not prescribe low sodium diets. Impurities in the drug have been responsible for alarming vasomotor reactions immediately after injection, but to date no harm has come from these. The possibility of adrenocortical derangement due to prolonged overstimulation has been kept in mind, although no proved in-

stance of hypoadrenocorticism has been encountered.

In all treated patients the process was arrested or regressed. In none of the patients treated during this early progressive stage did a partial or complete retrolental membrane develop. Some children now have normal fundi; some have a small mass of white tissue somewhere far in the periphery of the fundus. During the same period we have had 5 infants with progressing retrolental fibroplasia who did not receive ACTH for one reason or another. Two of them have now a complete bilateral membrane, 2 a partial membrane, and 1 has only a small mass of white tissue in the periphery of both fundi.

DR. BAIRD: We will ask Dr. Henderson if he will come back and answer some of these questions that we have received.

DR. HENDERSON: "Is it safe to use cortisone topically in ambulatory patients who are not under constant observation?"

To date I believe it is. Some patients can have cortisone administered topically at least every hour. The interval of administration is a matter of the consultant's judgment. If the patients are seen twice a week, that would be often enough. As these hormones become a little more available they will be useful for ambulatory patients. At the present time, I think that the scarcity of the hormones and the fact that they are so new is one reason they are asking that patients be put into hospitals. However, ACTH, in particular, stimulates all of the adrenocortical hormones, so that individuals must be watched not only for androgenic effects but also for the effect on blood electrolytes, protein and carbohydrate metabolism. Those people receiving ACTH over a period of more than a week have to be watched because of various systemic changes that are likely to occur.

"Has cortisone by injection been used in diabetic retinopathy?"

I think it has been. We have not used it ourselves. I do not know the result but I would be inclined not to use cortisone in any diabetic, for the reason that cortisone, as one of the adrenocortical hormones, has its most profound effect on protein and carbohydrate metabolism. If there is one thing that you need to watch in any patient receiving intramuscular cortisone, it is the blood sugar. The glucose tolerance curve is a better indication of the status of hyperglycemia in a patient receiving cortisone than is the blood sugar, but if neither blood sugar nor glucose tolerance tests are practical please keep watch on the content of sugar in the urine. If you are going to give cortisone to any diabetic, be sure of the cooperation of an internist. I would avoid giving cortisone to a diabetic if I could.

"In view of the effect of cortisone on hyaluronidase in the cornea, would this contraindicate prolonged topical instillation of cortisone?"

I do not suppose we know for sure how long one can give any drug, whether systemically or topically. The longest we have used topical administration in any one patient continuously has been about two months. I presume that, like all other new drugs and hormones, we will find many people who will not tolerate prolonged administration of cortisone. I presume this question concerning hyaluronidase will have to await the future for a satisfactory answer.

DR. MCLEAN: "Is there evidence that ACTH and cortisone interfere with fibroblastic proliferation sufficient to contraindicate parenteral or local use immediately after intraocular surgery?"

Our experience in that field is limited to paracentesis in secondary glaucoma while the drug has been continued. We have some slight indication that that may be the case, in that it has been unusually easy to reopen a paracentesis of the anterior chamber with a blunt spatula for days and days after the initial keratome or knife incision. We have not had the experience suggested by Dr. Henderson of doing major intraocular surgery under cortisone or ACTH therapy.

"Have you seen corneal edema from local cortisone?"

No.

"Have you used ACTH or cortisone in endophthalmitis?"

Yes. We have one case, the one I referred to under the group of unsuccessful cases, which started with an ulcer, developed into hypopyon, going on to endophthalmitis, and winding up with enucleation.

"What effect does cortisone have on thyrotropic exophthalmos?"

I have absolutely no experience on that subject.

"Do you know if cortisone affects the absorption of lens material after needling?"

I do not.

EXPANSION OF THE LUNGS IN THE NEWBORN: AN EXPERIMENTAL STUDY IN RABBITS

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and
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THE present study, though far afield from my clinical work, was undertaken at the request of some Duluth obstetricians with the hope that some light might be thrown on one of the causes of neonatal death. A review of the statistics covering a twenty-year period in our two major hospitals revealed that neonatal deaths had decreased materially during those twenty years from all causes with the exception of two, namely, malformations and abnormalities incompatible with life and atelectasis of the lungs. No great problems have been solved by our study but the members of the Academy who are interested in the respiratory tract may find something of interest in one phase of the subject, the physiologic expansion of the lungs in the newborn.

There have been many studies on atelectasis and a number on expansion of the lungs. Beck[1] reported upon 200 stillbirths and neonatal deaths, in which 41.5 per cent showed nothing more than congenital atelectasis. Labate,[8] in an analysis of the causes of death in a group of 868 stillbirths and neonatal deaths, listed pulmonary lesions as one of the three highest causes of death but did not mention atelectasis among them. Bell[2] has expressed the opinion that atelectasis is not the cause of death in most infants showing this condition but is merely an indication of weakness and debility secondary to other conditions which may cause death.

Potter and Dieckmann[10] reported upon a group of 17,500 infants with 25 deaths per thousand, equally divided between stillbirths and neonatal deaths. Twenty-five per cent of the neonatal deaths were attributed to prematurity. In these infants, the lungs were almost invariably red-purple in color, uniformly firm in consistency, and so airless that they sank in water. Microscopically they usually revealed resorption atelectasis. Most of these infants had breathed promptly after birth but within a few hours gave evidence of respiratory distress. They became progressively more cyanotic, even when kept in oxygen, and finally died of respiratory failure. This picture was almost always limited to infants weighing less than 2,500 grams. A similar thing happened in some of the experiments to be reported by us.

Wilson and Farber[13] did some excellent experimental work on the lungs of stillborn children and those dying shortly after birth, as well as on the lungs of living and dead animals. They concluded that atelectasis of the newborn should not be considered as a primary cause of death and that there must be some cause for the persistence of atelectasis. They found that a relatively great force was required to open the lungs the first time and decided that this resistance to expansion was due to cohesion of the

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moist surfaces of the collapsed air passages and the alveoli. They found that once the initial resistance was overcome, the lungs expanded with a much lower pressure. The initial resistance could be re-established by aspirating the lungs forcibly or by allowing them to hang for a number of hours. They pointed out that there is another type of atelectasis which is due to incomplete development of the lungs. They found that pressure of as much as 350 mm. of water might be required to produce full distention of the lungs in stillborn babies. (Adults use a force of only 10 to 20 mm. in quiet respiration.)

Smith[11] found that a pressure of 300 mm. of water may be necessary for expansion of the lungs in a stillborn. He stated that some degree of atelectasis may be demonstrable in normal infants for a week after birth. Potter and Adair[9] also expressed the belief that aeration of the lungs in a normal newborn was gradual.

Gruenwald[6] differentiated three conditions found in fetal lungs, namely, aerated, atelectatic, and a third which he called "fluid-containing." He expressed belief that fetal atelectasis is a normal state of the lungs just before birth. He reported that true atelectasis is much more common in liveborn than in stillborn children, and that the lungs of stillborns are much more apt to contain fluid because, in a period of anoxia, they have attempted to breathe in utero. Gruenwald measured the resistance of the lung tissue to expansion with both air and a watery fluid and found that the lungs expanded at a much lower pressure when fluid was used than when air was used. There was a more uniform expansion of the alveoli with fluid than with air. With the latter, expansion was not uniform: some alveoli expanded fully and others not at all. There was no intermediate stage. The author studied 30 stillborn infants and 30 newborn infants up to three days of age. He found that liveborn infants showed much less aspiration of amnionic fluid than the stillborns. He found commonly that some of the alveoli were aerated while others were partially expanded with fluid.

Zettelman[14] agreed, after some experimental studies on animals, that complete atelectasis of the lungs was maintained until birth unless there was some degree of anoxia. Amnionic fluid, he thought, was present normally in the larger air passages but was not normally present in the alveoli.

Farber and Wilson,[3] reviewing the literature concerning the nature of atelectasis in the newborn, concluded that expansion of the lung was not completed at the first breath but that it took several days and that a certain degree of initial atelectasis was physiologic for several days after birth. Areas of incompletely formed pulmonary tissue were frequently present in premature infants, they concluded, and this was not true atelectasis.

Weymuller, Bell and Krahulik[12] made roentgenographic studies of 25 normal babies during the first fourteen days of life. In only one was there evidence of atelectasis and this disappeared after twenty-four hours. Farrell[4] took roentgenograms of 159 infants within forty-eight hours of birth, most of them on the first day. No atelectasis was found in any. He stated that roentgenographically all of the lungs were fully expanded by the time the roentgenograms were made. On the other hand, Smith[11] cited findings from the Boston Lying-In Hospital that 18 per cent of the infants showed unexpanded areas in the lungs by roentgenography.

House and Owens[7] bronchoscopically examined 23 babies who had atelectasis. It is striking that 80 per cent of these babies were premature.

Gottschalk[5] reported a study on the results of premedication administered to mothers. He made a total of 68 records of the respirations in 40 infants during the first hour of life. The earliest was seven minutes after birth. Some of the mothers had received demerol and hyoscine, and others had not. The study indicated that demerol and hyoscine, no matter when administered, exerted no effect on the respiration of the newborn infant.

INITIATION OF RESPIRATION

Material

This study was made on rabbits. Ninety-nine fetuses from thirteen litters were used. The mother rabbits were killed by a blow on the head and the fetuses were delivered rapidly through an abdominal incision.

Position of the Fetus Within the Uterus

It was noted as each fetus was delivered that it lay within the membranes in the position of ventroflexion, which seems to be the usual position of unborn mammals.

Action of the Fetus After Delivery

The action of the fetus seemed to follow a characteristic pattern. If the rabbit was near term, as soon as the uterus was delivered outside the abdomen and manipulated, each little animal began to move and squirm. When removed from the uterus, it stretched out its hind legs and raked across the face and nose with the tiny claws on its forefeet, thus tearing the membranes and freeing its head. It then went into a position of opisthotonus and made gasping efforts for air, during which all of the accessory muscles of respiration came into play. If the animal was vigorous, respiration became established in a few seconds and it rolled about trying to free itself of the membranes. When free it got on its feet, sought its mother's fur and attempted to nurse.

If the animal was somewhat premature, it had difficulty in establishing respiration. It lay on its side gasping repeatedly and straining in the position of opisthotonus before breathing became established. If still more premature, it could not tear the membranes, either because its forelimbs were ineffectual and feeble or because that reflex had not yet been established. It had to be helped out of the sac and when free sought with great difficulty to get its breathing started. If it was sufficiently premature, respiration never became established. It gasped at intervals with the abdomen scaphoid and the ribs bending from external pressure; then the gasps became less and less frequent until they finally ceased entirely.

The Dissected Lung

If an animal which had established respiration readily was killed after a few minutes and the lungs dissected out, they were usually fairly well expanded. In some, however, portions remained atelectatic or unexpanded, even when the animal had been quite vigorous and apparently normal. It will be pointed out subsequently in this discussion that some animals, which one would expect from their activities had expanded the lungs well, under certain circumstances lost their vigorous breathing; respiration became progressively weaker and in some cases ceased entirely. In some of these the lungs were almost completely atelectatic and floated so heavily as barely to break the surface of water; others were completely collapsed, as though the animal had never breathed, and sank in water.

Most of the fetuses were killed by a blow on the head immediately upon delivery and while still within the amnionic sac. They did not breathe at all. These were the animals used for the pressure tests reported in another part of this paper. The entire respiratory tract below the larynx was dissected out intact,

the larynx cannulated and the lungs suspended in water and inflated. The inflation did not proceed evenly and progressively. Often the pressure was raised considerably before any air entered at all, and then it entered jerkily and irregularly. The distribution as the air entered was not uniform; one portion might suddenly pop into what looked like complete expansion before other areas received any air at all. In some instances, when the specimen was resting on the bottom of the pan, pinging noises were made as one patch after another suddenly expanded. One received the impression that the air made pressure against some sort of barrier, such as mucus, which would suddenly give way in the manner of a bursting bubble. Sometimes one lobe expanded more or less completely while an adjacent lobe remained completely collapsed.

Roentgenographic Studies in Infants

In a preliminary study made two years ago, several series of roentgenograms were taken of newborn babies, some before the first breath was taken, some twenty-four hours later and others on each of the first three days. There were 118 in the series which was x-rayed after the first twenty-four hours. Forty of these, about one-third, showed patches of unexpanded lung or atelectasis. Of those which were x-rayed on each of the first three days, about half showed unexpanded patches in one or more of the films.

These roentgenographic findings in babies, together with the findings in the dissected lungs of the rabbits which were allowed to breathe and the manner in which the unexpanded lungs responded to air pressure, all point quite definitely to the fact that expansion of the lungs is not a uniform process. Some areas may remain unexpanded for a period of time after birth.

Physics Involved in Expansion of the Lung

One must consider a number of physical factors in seeking to understand the manner in which the initial air enters the lung. Presumably all of the air passages, excepting the trachea and primary bronchi, are in collapse and the apposing surfaces in contact, with the probable exception of the thin film of fluid between them. The tubes are all small, the friction factor is high, and the resistance of capillarity and surface tension are comparatively great. In addition, there are the properties of the contained secretion to be considered, such as its viscosity and mucilaginous character. The resistance resulting from these physical forces is so great that a considerable pressure is required to overcome it. In the dissected lungs of these little newborn animals, a pressure of at least ten times that which we use in ordinary respiration (10 to 20 mm. H_2O) is required in order to float the lungs. Presumably the same would be true in the intact animal.

Presence of Fluid in the Respiratory Tract

There has been a great deal of discussion and difference of opinion as to whether fluid in the respiratory tract of the unborn is normal. In the fetuses used in these experiments, fluid was found in the tracheas of all of them; presumably there is a small amount of fluid in all of the air passages down to and including the alveoli. At least there is a tiny space of a few microns between the apposing epithelial surfaces in the unexpanded portions. It is not necessary to assume that this fluid is present as a result of inspiratory effort. The respiratory tract is a system of tubes which is open through the trachea. It is constructed while immersed in the amnionic fluid and it seems inevitable that some fluid must be contained.

PASSIVE ACTION OF THE THORACIC CAGE IN THE INITIATION OF RESPIRATION

Technic of Dissection

A definite method was developed in dissecting out the respiratory tract. The The fetus was laid on its back, a fold of the thin abdominal wall was grasped with a pair of rat-tooth forceps, then clipped with the scissors through the full thickness of the wall, as far as the xyphoid process. Still retaining a grasp on the incised fold of abdominal wall, the skin was dissected free from the anterior surface of the thorax and neck up above the larynx. In this maneuver, of course, the abdomen was opened widely. As the next step, the lower end of the sternum was grasped with the forceps and raised sufficiently so that the inferior surface of the diaphragm could be visualized. The ligaments of the liver were clipped through and the liver pushed inferiorly. At this stage, the lungs could be seen in apposition with the upper surface of the diaphragm and the thoracic wall, these structures being rather translucent. In the next step, the thoracic cage was opened by clipping across the lower ribs.

Following this, the breastplate was removed and the heart and respiratory tract, as high as the larynx, dissected out in toto. It was noted during this dissection that the instant the pleural cavity was penetrated, air rushed into the thoracic cavity. On opening the cavity fully, it was found that the lungs occupied only a small portion of it. In fact, as the air entered, the lungs appeared to collapse.

It seemed logical to assume that there could be only one explanation for this phenomenon. The animal had never breathed; therefore, the lungs must contain amniotic fluid which escaped through the trachea as air entered the pleural cavity, and the elastic lungs collapsed.

Two experiments were done to demonstrate the flow of fluid from the trachea. In the first, the trachea was exposed in the neck and dried. A dry glass slide was placed under it and the trachea was severed. When the thorax was opened, the lungs apparently collapsed, as usual, and the cut end of the trachea was watched for the outflow of fluid. But there was no flow of fluid. Another test was made on a second animal in a way which differed somewhat. The trachea was first tied off firmly, then the tract was dissected out and the whole specimen laid upon a dry slide. The trachea was then severed proximal to the tie. Again there was no flow of fluid, and this time the lungs did not collapse.

This seemed odd. The lungs occupied only a fraction of the volume of the thoracic cage and there was neither air nor fluid occupying the rest. What did occupy the remainder of the space? A little further study yielded the answer. When the unborn fetus lies in ventroflexion, the liver largely fills the thorax, forcing the heart into the apex and the lungs into the upper posterior portion. This could be readily demonstrated by dissection. In making these lung preparations, the liver was pulled downward in order to bring the diaphragm into view. This created a negative pressure in the thorax. Then, when the pleural cavity was opened, air rushed in and the ribs sprang away from the lungs, making it appear as though the lungs collapsed. When the liver was removed and the diaphragm opened, the thoracic cage expanded of its own elasticity. Presumably the ribs are built around the liver while the fetus lies in ventroflexion and thus are in the semi-expanded position all through prenatal life. When the animal first begins to breathe, it stretches out in opisthotonus and, by so doing, tends to pull the liver out of the thorax. This probably creates a negative pressure to assist in getting the first breath.

Further, the tendency of the ribs to spring to the expanded position enhances the ease of each subsequent breath. If the ribs were built while in the collapsed position, one would suppose that an added effort would be required to keep the thoracic cage expanded after breathing had been established.

Measurements were made on several animals to demonstrate the change in the girth of the thorax between the position of ventroflexion and that of opisthotonus. As the animal was straightened out, the girth of the thorax actually did decrease. It measured several millimeters less.

AIR PRESSURE REQUIRED TO EXPAND THE LUNGS

In these studies thirteen litters, with a total of 99 fetuses, were used. Of this number 33 fetuses were allowed to breathe and the remaining 66 were killed immediately within the amnionic sac before they had breathed. On 58 of these 66 fetuses, the pressure required to expand their lungs sufficiently to float them in water was measured.

Technic

The gestation period of a rabbit is said to be thirty-two days. The females were placed with a male a specified number of days (26 to 31) before the experiment was made. At the termination of this regulated period of time, the females were sacrificed and the fetuses delivered as rapidly as possible by abdominal section. The whole litter can readily be delivered in about two minutes. As quickly as the fetuses were delivered, those to be used in this study were sacrificed while they were still in the amnionic sac, as described above. The entire respiratory tract was removed intact from each fetus, dissecting from below upward. All of the tracheas were aspirated and then cannulated, and the cannula was attached to a water manometer.

Measurements were made on 58 fetuses to determine the amount of air pressure necessary to inflate the lungs. Over 300 determinations were made. It was learned on the first group of eight that "fully inflated" was not an exact term and that a definite end point of some kind would have to be established before the results would be comparable. Several end points were tried, but the one finally selected was as follows: The specimen, dangling from the end of the cannula, was sunk to the bottom in 20 mm. of water. Pressure was then made by means of either a glass or a rubber syringe through a Y tube, which was connected both to the lung specimen and to the manometer. A reading was taken at that point when the entire lung specimen just barely floated free from the bottom.

The average pressure required to float the lungs of 7 thirty-one day (near term) fetuses was 195 mm. of water. Forty measurements, varying from 118 mm. to 250 mm. of water, were made.

Effect of Prematurity

Thinking that prematurity might affect the pressure required, measurements were made on animals of various fetal ages. Thirty-three thirty-day fetuses required an average pressure of 194 mm. of water to float their lungs. The 128 readings taken on this group ranged from 91 mm. to 296 mm. of water. Six twenty-nine day fetuses required an average pressure of 197 mm. of water. Forty-two measurements were made on these 6 fetuses, ranging from 160 mm. to 260 mm. of water. Seventy measurements were made on 7 twenty-eight day fetuses. The average pressure required was 202 mm. of water, varying from a low reading of 140 mm. to a maximum of 300 mm. of water. Fifteen measurements were made on 4 twenty-six day fetuses, the average of which was 204 mm. of water and the range,

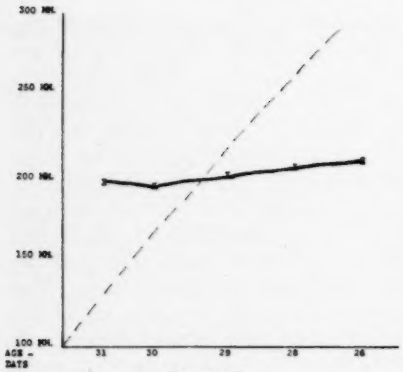

FIGURE 1

from 110 mm. to 250 mm. of water (fig. 1).

These figures indicate that although with prematurity there seems to be a slight increase in the average pressure required to open the lungs, it is probably not statistically significant. Since the range of pressures recorded varied rather widely (91 to 300 mm.) and since the number of animals was comparatively small, one cannot conclude that more pressure is required in the premature than in the term animal. Moreover, the degree of maturity did not seem to be uniform at a given number of days, i.e., some of the thirty-day litters appeared to be more premature than others of the same period of gestation, and even in a given litter some of the fetuses appeared to be more premature than others. The weights of the fetuses in the individual litters were found to vary as much as 50 per cent, the weights ranging from 33 to 48 grams. (Some littermates, which were not weighed, looked as though they varied even more.)

Relation to Weight

Twenty-three fetuses were weighed in an attempt to establish a relationship between the weights and the pressures required to float the lungs. The pressure required seemed to be about the same whether the weight of the fetus was 40 or 60 grams, and no correlation could be established (fig. 2).

Summary of All Pressures

Three hundred and two measurements were made on the lungs of 58 fetuses. The average pressure required to float the lungs was 193 mm. of water, under the conditions of the experiment. This comparatively great pressure, required to open the lungs initially, is made necessary by the resistance to inflation caused by the previously enumerated physical factors, which are not necessarily related to the size or age of the animal.

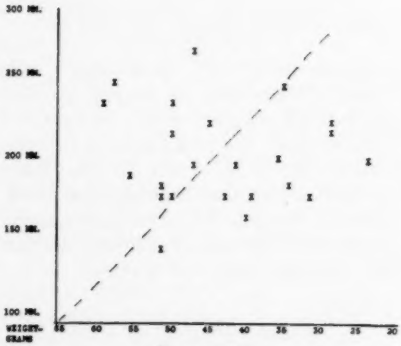

FIGURE 2

If these factors cause the resistance, then one would expect the initial measurements to be the highest and subsequent measurements, when the lungs had been partially or completely inflated, to be somewhat lower. This proved to be true. The first five determinations in 20 fetuses were averaged separately. The average pressure at the first determination was 210 mm. of water. The second reading was considerably lower, 194 mm. of water, and the average of the fifth measurement was 178 mm. of water. Other workers[13] have found a similar decrease in the pressure required to expand the lungs of stillborn babies after the initial inflation.

It is a striking thing that the lungs of such tiny animals require almost as much pressure to open them initially as do those of the human baby. Smith[11] found the pressure necessary to fully expand the lungs of a stillborn infant to be 300 mm., and Farber and Wilson stated that up to 350 mm. might be required. The average pressure merely to float these 58 rabbit fetuses was almost 200 mm.

SPONTANEOUS ATELECTASIS

After delivery, 26 fetuses were allowed to breathe for periods of time varying from twenty minutes to eighteen hours, following which they were sacrificed and their lungs examined. Spontaneous atelectasis or very incomplete expansion of the lungs was found in 13. In the other 13, the lungs were reasonably well expanded and floated high. Of the 13 with atelectasis, the lungs of 2 sank in water and appeared as though they had never been expanded. One of these animals was allowed to live for one hour and forty minutes, and the other for two hours and thirteen minutes. Soon after delivery both breathed and crawled, and one of them was described as being lively. In 2 other fetuses the lungs were so atelectatic that one lung sank and the other barely floated. One of these rabbits was described as having crawled and breathed well, but no description was recorded of the other immediately after delivery. All 4 of these animals were allowed to live more than one hour and forty minutes and all were feeble when sacrificed. There were 9 in which the lungs showed severe atelectasis or markedly incomplete expansion. These lungs all floated heavily and, in contrast to the pink color of the well-expanded lung, all showed a liver-like redness, which in some cases was diffuse and in others patchy.

Relation to Prematurity

This spontaneous atelectasis seemed quite definitely to be related to the degree of prematurity. Eight fetuses with a gestation period of twenty-nine days or less all showed complete or severe atelectasis when sacrificed. In none were the lungs well expanded. All 13 of those fetuses in which the lungs were pink and well-expanded and floated high were at the twenty-ninth day of gestation or beyond; 10 of them had reached at least the thirtieth day of gestation. The lungs which floated heavily came from animals scattered in fetal age all the way from twenty-six to thirty-one days, but most of them fell in the more premature group. There was only one exception to this general trend and that was in a thirty-one-day fetus (smaller than its two litter-mates) in which one lung sank and the other floated heavily (table I).

Possible Relationship to Chilling

An attempt was made to relate the spontaneous atelectasis to environmental temperature but this was inconclusive. Several animals kept at a temperature of about 40 F. developed atelectasis, but, on the other hand, some which were chilled to 30 F. and actually died of exposure did not show atelectasis. We do not doubt that in a large series of fetuses of the same age and weight a relationship between decreasing temperature and atelectasis might be demonstrated.

Possible Relationship to Swallowed Air

In dissecting the fetuses which were permitted to breathe, frequently we noted the stomach was greatly distended with air. In other words, the rabbits began swallowing air immediately upon breathing. The thought occurred to us that possibly the liver might again be forced up into the thoracic cage by the distended stomach, thus causing the lungs to collapse again. The total air content of a number of stomachs was measured but there did not seem to be any relation to spontaneous atelectasis.

TABLE I

PREMATURITY AND ATELECTASIS

SUBJECT	DAYS OF GESTATION	HOURS LIVED	DESCRIPTION OF LUNGS AT DEATH			
			BOTH SANK	ONE SANK	FLOATED HEAVILY	FLOATED HIGH
R-18	26	1⅔	F-8 *			
		½			F-2	
R-21	28	2¼	F-1 **			
		1½		F-2 ***		
		2			F-3	
R-2-50	28	– –			F-1	
					F-2	
R-9	29	3			F-8	
R-12	29	3½				F-5
		1¾				F-6
		1⅔				F-7
R-24	30	2½			F-1	
		2½			F-2	
R-7	30	⅓				F-1
		1				F-2
		2				F-3
		5 *'				F-5
		5 *'				F-6
		18				F-8
R-8	30	12 *'				F-10
R-6	31	1¾		F-7		
		1¾			F-6	
		1				F-5
R-9	31	3			F-8	
		¾				F-6
		3 *'				F-7
Total			2	2	9	13

*Breathed and crawled at birth; feeble at death.
**Lively, squealing and crawling at birth; breathing feebly at death.
***Crawling, breathing well at birth; feeble, responding to stimuli at death.
*'Found dead at the time specified.

Our pediatrician friends have told us that premature infants dying of atelectasis do not seem to have an inordinate amount of air in the stomach.

One premature infant, weighing but 625 grams at birth, was observed by one of us until it died at the age of three days. From 1½ to 3 cc. of air were aspirated at intervals but at no time was there any marked distention. Whether swallowing excessive amounts of air is related to prematurity, we are unable to state.

VISCOSITY STUDY

One of the original thoughts stimulating this study was that possibly premedication given to the mother might increase the infant's difficulty in expanding its lungs, especially when drying agents were used.

Study in Man

The first viscosity study concerns the respiratory mucus in man. Measurements were made on five volunteers, two of whom were used on two different occasions.

Technic. An instrument was devised for measuring the viscosity of respiratory mucus in the floor of the nose in situ. It consisted essentially of a small silver plate, 10 square millimeters in area, suspended at one end of a very

TABLE II

THE EFFECT OF ATROPINE ON THE VISCOSITY OF RESPIRATORY MUCUS IN MAN

NUMBER OF READINGS	SUBJECT	MG. / SQ. MM. OF RESISTANCE	PERCENTAGE OF INCREASE
27	CONTROL GROUP	9.2 (average)	
33	AFTER ATROPINE GR. 1/150	12.4	34
26	AFTER ATROPINE GR. 1/100 or GR. 1/75	17.7	92
59	ALL THOSE RECEIVING ATROPINE	14.9	62

light metal balance arm. This was mounted in an ear speculum on watch jewels at the fulcrum. In making the measurements, the little polished silver plate was pressed against the mucus on the floor of the nose and a measured weight moved out along the other arm of the balance rod until the silver plate lifted out of the mucus. The method was not entirely exact because a time element was involved just before the silver plate pulled free from the mucus. Nevertheless, an approximate measurement was obtained which could be repeated with reasonable consistency. The resistance measured was not that due to viscosity alone but was the resultant of several factors, among which were surface tension, the stickiness or mucilaginous property and perhaps also the Johansson phenomenon.*

The average of 27 control readings, before the administration of atropine, measured 9.2 mg. of resistance per square millimeter. After the administration of 0.4 mg. of atropine, 33 readings averaged 12.4 mg., or an increase of 34 per cent. Twenty-six readings, after 0.6 or 0.8 mg. of atropine, gave an average reading of 17.7 mg., or an increase of 92 per cent above the controls. Altogether, the 59 measurements, after the administration of atropine, indicated an average resistance of 14.9 mg. per square millimeter, or 62 per cent above that of the controls, indicating that the cohesiveness of the respiratory mucus can actually be increased by means of atropine (table II).

Study in Rabbits

The second viscosity study was carried out in rabbits. The drying agents (scopolamine or atropine) were injected into the mother and then measurements made on the fetuses, using the technic described under the section on the pressures required to expand the lungs. The drugs were administered to mother rabbits by hypodermic injection one hour previous to sacrificing them. The dose of scopolamine used was 0.4 mg. and of atropine either 0.1 or 0.2 mg. Forty-three determinations were made on 8 rabbit fetuses after the administration of atropine to the mother. The average of these 43 readings was 191 mm. of water, a rise of only eight points from the 183 mm. of water, which had been determined as the average pressure required to float the lungs in 5 control specimens. Twelve determinations were made on 3 specimens after the administration of scopolamine; the average pressure required to float the lungs was

*It will be recalled that the Johansson phenomenon is represented by the apparent tendency of two dry, smooth surfaces to adhere because air does not readily find its way between them and atmospheric pressure holds them together.

181 mm., or 2 mm. less than for the controls. In these few determinations, there was no indication that the administration of atropine or scopolamine increased the pressure which was necessary to open the lungs in the fetuses. These findings do not correspond with those we found in man. Many reasons for these apparent discrepancies come to mind."*

SUMMARY

This study describes the findings on 26 rabbit fetuses which were allowed to breathe and 58 which were killed before any breath was taken. The position of these rabbit fetuses within the uterus was that of ventroflexion; in this position, the liver occupies a large portion of the thoracic cavity in the unborn animal. The fetus throws itself into a position of opisthotonus and begins to gasp as soon as it gets its head free from the amnionic sac. This position may be purposeful in that it tends to pull the abdominal organs, notably the liver, out of the thoracic cage. The ribs tend to spring outward, thus making a negative pressure which presumably aids in initiating and maintaining respiration. If the thoracic cage were constructed closely around the unexpanded lungs, added effort would be needed to keep the cage expanded after respiration had become established.

Some of the animals which were permitted to breathe were killed while still vigorous; the lungs were well expanded in most of these but some showed patchy or diffuse areas of atelectasis. Some were allowed to live under adverse conditions, such as chilling, until they became quite feeble. Many of these showed more or less complete atelectasis. In two the atelectasis was so complete that it looked as though the animals had never breathed and yet they had crawled about quite vigorously immediately after delivery. Apparently these animals with atelectasis were unable to maintain their lungs in expansion. The causes of this are not clear excepting that the degree of prematurity seemed to be a fairly definite factor. Most of the instances of severe atelectasis occurred in the more premature animals.

The respiratory tract was dissected out of the 58 animals which were killed before breathing and the lungs subjected to a measured pressure in order to determine how much was required to expand them to the point where they would float. The pressures required to open the lungs of the rabbit fetuses were comparatively great, being in the neighborhood of 200 mm. of water. The variation was rather wide but the averages at the different ages and weights were essentially the same. There was no indication that the pressure required was greater in the more premature animals than in those at or near term. One would assume that the resistance offered to the incoming air is a matter of physical factors such as the small diameter of the air passages, the high friction factor and the characteristics of the contained secretion rather than the age and weight of the animal. It is interesting to note that the pressure required to expand the lungs in these 50-gram animals was almost as great as that recorded for human babies. One wonders if it would be much greater in an elephant.

It was observed during these determinations that the air did not enter uniformly; it entered in a jerky fashion and the lungs expanded most irregularly. This probably explains the fact that some degree of atelectasis was found in

*Perhaps the rabbits are not greatly affected by these drugs; perhaps the scopolamine does not reach the fetus, at least in one hour; maybe the fluid in the bronchial tree prevents an increase in cohesiveness of the mucus; probably the number of measurements made was too low to be statistically significant; although both sets of measurements were made in the respiratory tract, conditions are very different in the anterior portion of the nose from those in the bronchioles and alveoli; the two species are markedly different, as are the physiologic ages.

the roentgenographic studies of newborn infants, both in our series and in those studied by others. There seems to be no reasonable doubt that the lungs in a newborn do not expand fully immediately after birth. The process is progressive during several days.

A few experiments were made to test the relationship between drying agents given to the mother and the pressures required to open the lungs of the fetus. There was no indication in these experiments that the drying agents increased the pressure required but, for many reasons, this result must remain inconclusive.

A review of the literature indicates that our studies resulted in no new information unless it might be that of the action of the liver and thoracic wall in initiating respiration. The findings corroborate those of other workers who maintain that complete expansion of the lungs is a process which takes several days. Spontaneous atelectasis was produced a number of times but the cause is just as obscure in these animals as it seems to be in the human baby. Our study, like reports of others in the literature, indicates that prematurity is a definite factor.

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DISCUSSION

PAUL H. HOLINGER, M.D., Chicago, Ill.: The term "atelectasis" is derived from two Greek words meaning imperfect expansion. In present day use, three types of atelectasis have been recognized; one due to bronchial obstruction with absorption of air distal to the obstruction, a second due to pneumothorax and collapse of the lung, and the third, the type Dr. Hilding has just discussed, the imperfect expansion of the lungs at birth. One of the most significant points mentioned in the discussion seems to be the recognition of the kicking mechanism which brings the fetus into the opisthotonus position. The pull of the liver on the diaphragm and the spring action of the ribs apparently aid in expansion of the lungs in a very direct manner. From a clinical standpoint this would aid in explaining the imperfect expansion of the lungs in the weak, flaccid premature child and in the infant with a cerebral birth injury who has lost the muscular activity and reflexes of the

extremities. That the pull on the diaphragm by the liver is significant can be demonstrated in many ways in airplanes and elevators; experimentally, the sensations from quick starts and stops in an elevator can be reversed if one stands on his head in an elevator, as we did some years ago with Dr. Ivy to test this effect.

As Dr. Hilding well knows, a measure of the pressure necessary to inflate the lungs of a newborn is not a direct measure of the ability of the infant to survive even though the mechanism is available to supply that negative pressure. Other factors, such as the full, final development of the lung tissue itself, must be present. It is for this reason that prematurity is such an important factor in atelectasis of the newborn. Areas of incompletely formed pulmonary tissues may take days or weeks to reach maturity and may or may not eventually expand. That expansion of the lungs immediately after birth is a gradual, jerky process requiring several days is an important clinical point. Just now considerable pressure is being placed on the bronchoscopist to "do something," such as bronchoscope an infant, if partial atelectasis is demonstrated. Obviously the clinician cannot differentiate between atelectasis due to incomplete development of the lung and atelectasis due to the failure of normal lung tissue to expand because of failure of the kicking mechanism. If roentgenograms demonstrate areas of atelectasis and physical examination reveals the presence of mucus in the trachea and major bronchi, aspiration may be indicated. But the presence of a cerebral birth injury as evidenced by the complete flaccidity of the infant may be a contraindication to anything but pharyngeal aspiration to avoid further brain damage.

In closing the discussion of this extremely interesting and timely paper characteristic of Dr. Hilding's fundamental research work, I should like to ask how it was determined that in some fetuses atelectasis was produced after birth? How did these lungs differ from those that had failed to expand initially?

JAMES L. WILSON, M.D., Ann Arbor, Mich. (by invitation): As a pediatrician I am, of course, very pleased that this society should interest itself in this fundamental work which has been a matter of great interest to me for many years. I can say right off that my own clinical observations and studies which I also made on rabbits many years ago fully confirm the work of Dr. Hilding. I can agree with all his conclusions.

I might summarize very briefly and perhaps dogmatically my own opinion about some of these points which still need further study. I think everyone is agreed that intrauterine respiration takes place. There is difference of opinion as to how effective it is. In other words, how much tidal flow of fluid occurs, and how much are the lungs really expanded by the rather violent intrauterine efforts that can be observed. I made some observations on this point once which I have not published. These experiments were also carried out on rabbits. Cesarean sections were done and the fetuses delivered into a warm saline bath. They were seen to struggle, to kick and to breathe just as has been so vividly described by Dr. Hilding. I put over their snouts a little watertight attachment, which I won't take time to describe, by which I could measure directly the flow of fluid. These animals quite obviously violently struggled to breathe, looking much like premature infants that I am familiar with, with their diaphragms contracting vigorously. With a great many observations I never found one where the flow of fluid in and out of the apparatus could be more than one tenth of a cubic centimeter, which even in such a small animal is nowhere near enough to expand the lungs.

The first breath of life after birth is certainly one of the most difficult, if not the most difficult one, that ever occurs. It is logical, therefore, that we can expect more trouble with premature babies. Not only do they have less well developed reflexes and respiratory centers but their muscles are also less well developed, and they possess a flexible thoracic cage which gives in to rather than opposes the diaphragm.

One other factor which has been thoroughly established has been mentioned. The lungs of the premature infant are to a considerable extent simply unexpandable. I have observed them living as long as six weeks with practically no fine alveoli, as such, demonstrable at time of death.

It is inevitable that the first breath aspirates amniotic fluid further into the lungs. Such fluid is already in the trachea and larger bronchi. We cannot imagine that these lungs remain in utero in a state of vacuum, of course, or that suddenly all the fluid is drained out by obstetrical technics at the moment of birth. This amount of fluid, ordinarily at least, cannot greatly handicap the baby, and we can see how by expansion of the lungs their internal surface is enormously increased, so that the relatively small amount of fluid is so thinly spread as ordinarily to constitute no barrier

to gas exchange. There can be exceptions to this, of course. However, in the experimental work I was engaged in years ago we were never able to demonstrate very clearly that material in the air passages was the explanaplanation for atelectasis.

As the two previous speakers have emphasized, I think we can state that atelectasis should not be considered a primary cause of a baby's failure to do well, any more than an empty gut should be considered the cause of death in a baby who has intestinal obstruction. The cause of the atelectasis is the thing to which we should direct our attention and we need to direct a great deal more to it.

I wish physicians with your technics could make further studies. I am fascinated by the work of Dr. Hilding in beginning to study the viscosity of secretions by the technic he has developed. I am sure something more can be learned by that technic.

The function of the larynx also needs more observation. Why is it that a doctor may have no success with a baby that breathes with obvious effort and with signs of respiratory obstruction and has a very poor air exchange even though the child is placed in a machine for artificial respiration by which the negative inspiratory pressure is raised up to the point at which an excised lung would be easily expanded, according to Dr. Hilding's research? I wonder if there is some neurological problem involved, with poor functioning or spasm of the larynx, that prevents recovery from fetal atelectasis and interferes with efforts to increase the tidal air. This same factor may occur in intrauterine life and prevent a free flow of amniotic fluid.

DR. HILDING: I want to thank the discussers for their kind remarks.

I inadvertently omitted from my paper one point which I wish to make, namely, the comparison of the girth of the thorax in the positions of ventroflexion and full extension of the body. Comparative measurements in these two positions were made in a number of animals. It was found in all that the girth of the thorax was several millimeters less in the latter than in the former position.

As Dr. Wilson said, there is no apparent reason why some of these animals and some babies develop atelectasis after they have breathed for a while. When death occurs in the presence of atelectasis, atelectasis does not seem to be the cause. In the case of these animals, we thought that perhaps adverse environment might favor atelectasis because the first spontaneous atelectasis which we found occurred in some animals that had been chilled. More were chilled under controlled conditions and atelectasis did occur in some of these, but not regularly. In fact, some which were exposed at freezing temperatures until they died did not develop atelectasis.

Dr. Holinger asked if the lungs in those which developed spontaneous atelectasis differed from those which did not open at all. Grossly they did not. We have not completed the microscopic studies, so I cannot answer that question. As both Dr. Wilson and Dr. Holinger indicated, lungs which are not fully developed will not expand at all.

Dr. Wilson mentioned the fluid in the trachea and the fact that this is aspirated. There has been one experimental study which is mentioned in the review of the literature in which a comparison was made between the pressure required to expand the lungs with air and with watery fluid. It was found that they expanded with watery fluid at much lower pressure than with air, so it may be that this small quantity of amnionic fluid present in the larger air passages is purposeful. It may aid in breaking the barriers of surface tension to get the first air in.

Thank you very much.

TREATMENT OF DEAFNESS BY MECHANICAL PROSTHESIS

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EVER since the beginning of medicine there has existed a branch of the healing art which aimed to replace lost parts of the body. Patients with an amputation of leg or arm, a lost eye, a defect in the palate, or missing teeth are in need of a prosthesis. In some cases the prosthesis fulfills a cosmetic function only, as in the case of an artificial eye. More frequently, however, the attempt to restore normal appearance is combined with an effort to replace the function of the lost organ.

In otology the attempts to restore the function of destroyed parts of the ear have been made over a long period of time.

In 1640 Marcus Banzer[2] published a paper on hearing defects and the treatment of deafness. In accordance with the customs of his time, the language of his publication was Latin: "Disputatio de auditione laesa" is its title. In the paper, Banzer advises the use of a small tube of elk's claw which is covered by a pig's bladder at its end. A century later in 1763 Leschevin[8] reported on the use of an artificial ear drum. In 1815 Authenrieth and Bohneberger[1] proposed their artificial ear drum for the improvement of hearing. In spite of a series of favorable reports by Ward Deleans and Tods,[9] the method was not adapted generally until Toynbee[14] in 1852 introduced the artificial ear drum which for a long time carried his name.

A wave of enthusiasm followed Toynbee's publication because lay people expected from this prosthesis the same therapeutic possibilities that glasses provide for the eye. Needless to say, the expectations were not fulfilled. In certain cases there was a striking improvement of hearing. However, the disadvantages and restrictions of the method soon became apparent. The prosthesis irritated the delicate tissues of the middle ear. Secretion recurred or increased in amount. Noises due to mastication, to talking or to spontaneous shifting of the instrument were bothersome. Ever since the original conception of the method, physicians have tried unsuccessfully to overcome the difficulties.

The most recent attempts were made by the Pohlmans.[10,11,12,13] Again as in Toynbee's days a wave of interest and enthusiasm is sweeping the country, finding its climax in a publication in *Life Magazine*. But let us learn from history. Too great promises are bound to be followed by disappointment, disappointment among both the laity and the medical profession. An objective detached appraisal seems in order. More information is vitally needed. The otologist should be interested because here is available a variety of very simple but astonishingly effective methods which improve the hearing of the patient. The physiologist is bound to gain new information about the function of hearing. Every patient treated with an acoustic prosthesis represents an experiment on the physiology of hearing.

Definition of Terms

A hearing prosthesis is defined as any device which replaces the function of a part of the sound conducting system of the ear. An electric hearing aid is not a

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prosthesis in the strict sense because it functions on the principle of increased stimulation and not on the principle of improved ear function. One can distinguish three types of hearing prostheses.

1. Devices which close a perforation of the ear drum (ear drum prosthesis)
2. Devices which are attached to certain parts of the medial tympanal wall, mostly in the round window or stapes area (tympanal prosthesis)
3. Prostheses which aim to replace a destroyed ossicular chain (ossicular prosthesis)

A PERFORATION OF THE EAR DRUM: ITS EFFECT ON SOUND CONDUCTION

The physical effect of a drum perforation in the ear is difficult to ascertain. Recent biophysical experimentation has changed the concept of this disease.

Let us consider a dry, central perforation with no active inflammatory processes in the middle ear and no destruction nor adhesions of the ossicles. A central perforation means that a direct air communication exists between the outer ear canal and the middle ear cavity. Sound energy can reach both the inner ear windows directly. The conventional explanation of the condition is about as follows:

The movements of the stapes footplate produce oscillations in the intralabyrinthine fluid. When the stapes moves inward the round window moves outward. The oscillations of the round window membrane are the sum of the vibrations of the intralabyrinthine fluid and direct sound conduction through the air of the middle ear. Since the two are in nearly opposite phase, the aerocochlear conduction impedes the movements of the round window membrane and thus diminishes the intralabyrinthine oscillations.

Modern physical concepts show, however, that the acoustical conditions are much more complex. First of all, one has to place more importance on the air of the middle ear cavity. The air content of the middle ear is an important structure of the ear, but since it is invisible, since it does not stain with our histologic technics, it is, in the mind of the otologists, just about nonexistent. However, modern physical experiments have proved that the air of the middle cavity has a very definite physical effect. Békèsy[3] has published experimental data in which he showed that for frequencies up to 2000 the ear-drum membrane owes its physical behavior not to its own elastic qualities but rather to the elastic qualities of the bubble of air encased behind it in the middle ear space. The air bubble acts like a spring, has its characteristic elasticity and dampening. The acoustic physicist is accustomed to the effect of air encased behind a vibrating membrane. The designers of microphones purposely place some air behind the vibrating microphone plate. The otologist deals with a similar system.

The perforation of the ear drum assumes now a completely new aspect. The destruction of ear-drum tissue is not the important factor, but rather the formation of a communication of the middle ear air with the outside world. We can, perhaps, describe the physical effect of an ear-drum perforation as follows: The system of an encased air bubble is changed to an open system best compared with a Helmholtz resonator.

The therapeutic effect of the artificial ear drum has now a different meaning. It is not used to replace destroyed drum tissue. Whatever material we use, be it gutta-percha, fish skin, rubber membrane, cotton, gauze or even only a drop of fluid, the effect is the same: the air bubble of the middle ear cavity becomes encased again.

Figure 1 is the audiogram of a patient with bilateral chronic otitis media. This patient learned to place cotton, rubber

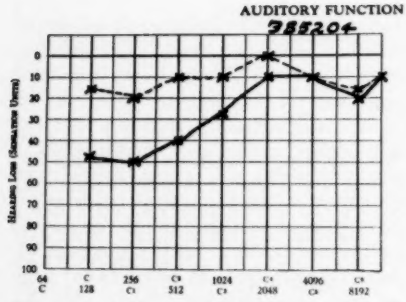

FIG. 1—Mr. S. Central perforation in anterior half of drum membrane. Solid line indicates unaided hearing by air conduction. Interrupted line designates improved hearing threshold obtained by closing the perforation with a rubber membrane. NOTE: Hearing gain greatest for low tones; maximal improvement, 35 db. No improvement for high tones.

or cigaret paper over the perforation. The hearing improvement is good for the low and middle ranges but is absent for high tones.

A motion picture film is shown demonstrating a normal ear drum, an ear drum with perforation and closure of perforation by rubber membrane and cotton pledget. The acoustic oscillations of the ear drum and of the artificial ear drum are shown.

TYMPANAL PROTHESIS

In cases of middle ear diseases in which ear drum, malleus and incus have been destroyed, the stapes and round window membrane are both facing the sound waves. The preferential conduction to the oval window, which is normally accomplished by the ossicular chain, is not present in such an ear; the opinion was brought forward long ago that some material brought into the round window niche acts as a screen and keeps the sound energy from reaching the round window membrane. A very characteristic term has been used for this procedure. It has been said the round window is placed into "sound shadow." Prerequisite for the condition is that a bubble of air be left between the cotton pellet and the membrane of the round window. According to this concept, the air bubble will permit excursions of the membrane during acoustic stimulation of the ear but prevents the sound from reaching the round window directly. The clinical evidence as to the effectiveness of a cotton pellet is convincing. However, the interpretation of a sound shadow is questionable on physical grounds.

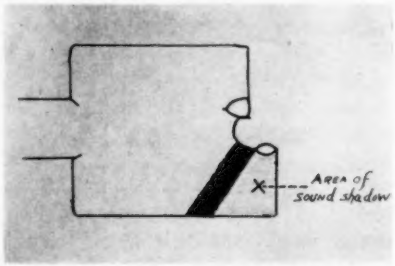

FIG. 2—Sketch of middle ear. Ear-drum defect, loss of malleus and incus. Demonstration of the effect of a cotton pellet which obstructs the round window niche but is not in direct contact with the round window membrane. The pellet is thought to absorb or reflect nearly all sound energy which impinges on it. The area behind the pellet has been described as a field of sound shadow. Hearing improvement is based on elimination of round window conduction.

The cotton pellet is also effective if no air is left in front of the round window membrane. If a drop of oil or mercury is placed straight against the membrane, a good hearing improvement is obtained also. Furthermore, if the foreign body is placed against the stapes, a similar hearing improvement is found. It is evident that the physical conditions in such a case are different from the "sound shadow" effect. The physical effect of the pellets is the same on either stapes or round window membrane. It acts like an increase of the mass factor. The law of mechanics pertaining to resonance of oscillating systems should be applied in this case. Suppose a vibrating system has the resonance shown by curve 1 in figure 3. Its resonance frequency is determined by the stiffness and mass of the system. Since the mass is the denom-

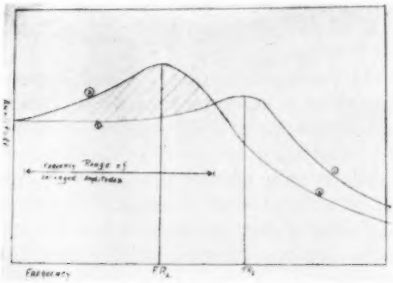

FIG. 3—This scheme demonstrates a possible explanation for the improvement of hearing observed when a cotton pellet is placed against the stapes or the round window membrane. Abscissa: frequencies; ordinate: recorded amplitudes.

Curve 1 demonstrates the resonance curve before insertion of the pellet. Its resonance lies at FR_1. Curve 2 designates the resonance after insertion of the pellet. According to the laws of physics, the increase of mass causes a shift of the resonance to a lower pitch (FR_2). It is assumed that the new resonance point lies in a frequency range which is close to the important speech frequencies. Shaded field represents area of hearing improvement. In the high tone area, hearing is actually impaired by pellet. However, this area is unimportant clinically because it is above speech frequencies.

inator of the fraction, an increase of mass will result in lowering the resonance frequency. The insertion of the pellet increases the mass factor. The curve shows that the resonance frequency shifts toward the left, that is, toward a lower frequency. This is not the only result. It is also evident that the amplitudes of the lower frequency range will increase. The effect of the mercury drop or the oil-soaked pellet can, therefore, be explained as an increase of the mass factor, resulting in a lower resonance frequency and greater amplitude of the lower frequencies. It is also explained why placing the pellet on the stapes and on the round window membrane has the same effect. The loss of the conduction of higher frequencies is irrelevant if these frequencies are above the speech range. The effect of a tympanal prosthesis on hearing is shown in figure 4.

[Demonstration of a motion picture film on the insertion of the round window plug and its physical behavior during sound reduction.]

OSSICULAR PROSTHESIS

If a man loses a leg, a prosthesis is given to him to replace his limb. A logical consequence for the otologist is when a man loses his ossicular chain to replace it by a prosthesis. At this time it is only right to give credit to a man who has, without being an otologist, worked a lifetime on the problem of hearing. His

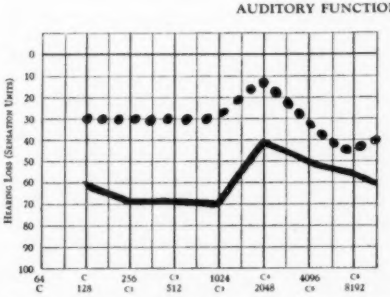

FIG. 4—Mr. J. T. Effect of tympanal prosthesis (cotton pellet) on auditory function. Remarkable improvement for low tones (40 db.) while high tones show less improvement. The hearing gain was obtained either by placing the pellet against the stapes or by pressing it tightly into the round window niche.

effort revived the interest in hearing prostheses and many patients have benefited by his work. Augustus Pohlman[10,11] deserves due credit for his studies and for the creation of the Pohlman prosthesis. Pohlman does not claim that the prosthesis is a new idea, but there is no doubt that his theoretic investigations and his technic of making the prosthesis have benefited the otologic profession.

Marcus Banzer in his "Disputatio de auditione laesa" recommended the claw of a deer covered at its end by pig's bladder. In 1938, just about 300 years after Banzer, Pohlman's recommendation was pig's bristle with fish skin; in 1950, *le dernier cri* of the otological prosthesis vogue is nylon instead of pig's bristle.

The present Pohlman technic entails making a mold of the outer ear canal, and the fashioning of an individual insert with a silver ring for maintaining the tension of the membrane. This advanced technic requires cooperation with a dentist. Various mechanical difficulties have prevented the wider usage of the prosthesis. Pohlman's original technic is much simpler and is satisfactory in many cases.

The two ends of a 00 gelatin capsule are punched out with a beaked cork borer and the two parts of the capsule separated. A bit of moistened fish skin condom is pressed into the larger segment of the capsule, the smaller segment being employed as a plunger. When dry, the diaphragm thus produced is shellacked to make it somewhat stiffer and moisture proof. The columella of a bird is imitated by melting a small head of dental stent on the end of a stout boar bristle. The free end of the bristle is fed through a hole pricked into the diaphragm with a needle. The capsule is seated into the bony external canal and the bristle is gently pushed into contact with the predetermined yielding area.

The contact area essential to the proper application of the prosthesis is very critical. Before using the diaphragm rod prosthesis it is, therefore, important to determine the existence, the site and sensitivity of the yielding point. This determination is made with a simple device which is called the acoustic probe. The acoustic probe consists of a mica diaphragm with an attached slender rod (bamboo is a suitable material) as a handle. The probe is held by the handle, and various parts of the medial tympanal wall are touched while a constant sound is given as a test tone. Incidentally, due to the low natural frequency of the mica diaphragm, a considerable distortion results. The most important speech frequencies show the most improvement; the low frequencies, which frequently contain some disturbing noise, are filtered out. An improvement of 30 db. is frequently observed; the greatest improvement reported was 60 db. for 1024.[7]

[Demonstration of slides and motion picture demonstration of Pohlman prosthesis.]

In summarizing, the following practical procedure is recommended. When a patient has a considerable loss of hearing due to a conduction lesion, the possibilities of a hearing prosthesis should be considered. First, it should be learned from the history whether or not the patient has spontaneous improvement of hearing. Fairly frequently, a drop of secretion can act as prosthesis and produce hearing improvement. Cases of unexplained sudden but only temporary improvement of hearing should be investigated systematically for the best and most permanent improvement of hearing. The term "systematically" is used advisedly because most cases in the past have been subjected to only a few attempts, without a definite plan of procedure.

When there is a dry perforation of the ear drum of moderate size, a closing by fish skin membrane has the greatest chance of success. However, a more weighted, cotton pledget soaked in oil should be used, too, if and when the first method fails. Self application by the patient can be easily taught provided the patient has interest enough and is fairly skillful.

The tympanal prosthesis requires the greatest skill and perseverance in fitting. Again the history of spontaneous hearing improvements is important. The otologist should investigate whether or not yawning has the tendency to improve hearing even for a short time. A systematic study of pellets should be carried out. The size of the pellet may be of little importance, but the exact position may be critical. One should insert the pellet and expose the patient to a constant sound. One may play the radio or one may keep talking continuously into the ear of the patient. The pellet is then moved around with an ear

hook. If direct contact with either the stapes or the round window fails to give results, one should try a loose cotton pellet placed in contact with the tympanal wall but providing an air space in front of the round window membrane. The necessity of changing the prosthesis daily must be considered a greater disadvantage. Many patients are not interested enough or not skillful enough to place a prosthesis properly in their middle ear. Experiments are being carried out to find inert materials which can be left in the ear for longer periods.

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INDUSTRIAL ACOUSTIC TRAUMA

DOUGLAS E. WHEELER, PH.D.
LOS ANGELES, CALIF.

THE incidence of industrial acoustic trauma has long been known to the otologic profession. Recently, however, more attention has been directed toward the problem. Within the past year, a Conference on Noise in Industry was conducted by representatives of two well-known and active organizations. The first of these is the Committee on Physical Agents of a Hazardous Nature, a standing committee of the Congress on Industrial Health of the American Medical Association; the second is the Sub-Committee on Noise in Industry, a division of the Committee on Conservation of Hearing, The American Academy of Ophthalmology and Otolaryngology. Following is a brief quotation from the findings of this conference:

It was felt that emphasis on the problem of industrial acoustic trauma is particularly needed at this time because:

1. The use of equipment which generates high noise levels is increasing in industry, with consequent exposure of more workmen than previously to definitely injurious sounds.
2. Activity has increased recently with respect to compensation claims for impaired hearing.
3. The possibility exists that the hearing of some persons may be affected adversely by long-continued exposure to noise below the levels of intensity generally regarded as potentially injurious.

Among the several courses of action required in the attack on industrial acoustic trauma, certainly one is the accumulation of a systematic, quantified body of information. Certain data can be, and have been, contributed from the laboratory, but the most important area of study is that of industry itself. For more than a year the Sub-Committee on Noise in Industry has maintained a program of active field research; this research has already been accepted and facilitated at representative locations by the shipbuilding, aircraft, and weaving industries. It now appears that in the near future the program may be extended to include the railroads and other industries engaged in the fabrication of heavy metals.

Such field research is potentially capable of three objectives:

1. The accumulation of quantitative information
2. Distribution to otologists of relevant information which may be of assistance both in diagnosis and prognosis
3. The arousal of interest and concern among those in the industrial plant whose responsibility is to deal with working conditions, namely, industrial relations personnel, safety engineers, industrial hygienists, and medical departments

The latter point, that is, arousal of interest and concern, requires some emphasis. Industry, at the present time, is understandably apprehensive in the presence of what seems to be a new industrial hazard. Actually, of course, it is not new; on the other hand, however, it is poorly understood.

In an effort to place in appropriate industrial hands a realistic evaluation of this hazard as it typically exists, the Sub-Committee on Noise in Industry has produced a motion picture. This is a short film; it does not deal with all the ramifications of the industrial acoustic

Presented at the meeting of the Committee on the Conservation of Hearing, Oct. 8, 1950, Chicago, Ill., in connection with a showing of the motion picture film "Your Ear and Noise."

hazard, a widespread and complex problem. It is the purpose of this picture to describe the conditions likely to produce acoustic trauma, the instruments and measurements required to detect both the existence of the hazard and its auditory effects, and, lastly, certain remedial procedures which the Sub-Committee on Noise in Industry regards as reasonably practical at the present time.

The title of the film is "Your Ear and Noise."* A circular regarding it, gives the following description:

This motion picture is about noise and the effects of noise upon hearing. Noise may affect personality, temperament, and efficiency, and definitely produces undesirable changes in hearing acuity in certain sensitive individuals.

This picture:

1. Describes the characteristics of noise.
2. Suggests limits beyond which noise becomes hazardous.
3. Shows ways in which hearing is affected.
4. Points out means for detecting damage in early stages.
5. Mentions instruments for locating noise hazards.
6. Illustrates types and uses of ear protectors.
7. Recommends pre-employment and periodic hearing tests for combating this problem.

The noise hazard, in common with other industrial hazards, has limits. In industry, only those exposed to noise above certain levels are endangered; therefore, this hazard *can* be controlled. Methods and types of control vary with the particular situation and should be studied by employee relation officers, safety engineers, industrial hygienists, and all other management personnel concerned with hazards to industrial health.

*This picture is issued by the American Academy of Ophthalmology and Otolaryngology, through the Sub-Committee on Noise in Industry of the Committee on Conservation of Hearing. All inquiries regarding it should be sent to Dr. Douglas E. Wheeler, Field Representative of the Sub-Committee on Noise in Industry, 1136 West Sixth Street, Los Angeles 17, Calif.

HOME STUDY COURSES

The 1951-1952 Home Study Courses will begin on September 1 and continue for a period of ten months. Requests for registration should be made before August 15.

If military assignments interfere with the completion of these Courses, upon request such registrations will be transferred to a future date without the payment of additional fees.

Detailed information and application forms may be secured from Dr. William L. Benedict, 100 First Avenue Building, Rochester, Minnesota.

In Memoriam

Ellery Leslie Armstrong.....Duluth, Minnesota
January 2, 1951

Harry Lester Baum.....Denver, Colorado
April 25, 1951

Eugene Augustine Curtin.....Scranton, Pennsylvania
January 7, 1951

Ralph Ferrien Davis.....Portland, Oregon
February 8, 1951

Joseph Ivimey Dowling.....Albany, New York
March 21, 1951

Warren Reynolds Hickman.....Logansport, Indiana
January 29, 1951

Alexander A. La Vigne.....New York, New York
October 31, 1950

John Miller.....Greenwich, Connecticut
January 14, 1951

Herbert Moulton.....Fort Smith, Arkansas
January 23, 1951

John James Prendergast.....San Diego, California
April 8, 1951

John Christopher Rommel.....Narberth, Pennsylvania
January 14, 1951

TRANSACTIONS

American Academy of Ophthalmology and Otolaryngology

Official Publication of the American Academy of Ophthalmology and Otolaryngology

Published under the direction of the Editorial Board

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HENRY L. WILLIAMS, Rochester, Minnesota, *Associate Editor*

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All communications regarding the TRANSACTIONS should be addressed to William L. Benedict, M.D., Executive Secretary-Treasurer, the American Academy of Ophthalmology and Otolaryngology, 100 First Avenue Building, Rochester, Minnesota

Editorials

MOTION PICTURES

The use of audiovisual aids in medical schools and in hospitals has grown rapidly during the past four years. A recent survey made by the A.M.A. Committee on Medical Motion Pictures reveals some interesting facts on the number of films used in teaching and the facilities for projection of films and slides.

Nearly all medical schools now own motion picture projectors or have them readily available and use curriculum-integrated films in many of the preclinical as well as in the clinical courses. In all hospitals and in medical centers of the armed forces, audiovisual aids are regularly used in classwork and in seminars. The use of telecasts and kinescopes has been introduced for closed circuit and public showing in at least forty-five television communities and has been well received (J.A.M.A., 146:479-480 [June 2] 1951). Televising of medical clinics and surgical operations has been repeatedly demonstrated at medical conventions. The cost of such televising is far beyond the reach of most medical school budgets, but one manufacturer of television equipment is said to be making twelve sets of telecast material on various medical problems for use in medical schools.

Teachers make use of motion pictures in various ways. As better and more adaptable films are made available, they will be used to supplement clinical demonstrations of patients and clinical lectures. They are not recommended as substitutes for lectures. Many teachers probably do not get as much help from motion pictures as is possible because of their infamiliarity with their use. One experienced teacher has advocated "an institute of visual education where the visual arts, crafts and sciences of medical communication can be taught under ideal conditions." A well-controlled curriculum research study will be made in one or more of our medical schools in order to measure the effectiveness of motion pictures as an educational tool.

The Committee on Motion Pictures of the Academy has taken a long step forward in the production of "The Embryology of the Eye." This production has won warm words of praise from many reviewers, and prints have been purchased by many medical schools, medical societies, and individuals. When used with lantern slides which have been made from key pictures in the film, the

general conception of the development of the human eye becomes more realistic than any other method of study permits.

The wide acceptance of "The Embryology of the Eye" by teachers and practitioners is most encouraging. Naturally the making of a similar film on embryology of the ear is urged, as it will be equally useful in the teaching of otology. Other films are contemplated, probably on a smaller scale, as curriculum-integrated visual aids on basic as well as clinical subjects. The Academy committee works closely with the committees on motion pictures of the American Medical Association, the American College of Surgeons, and with the Medical Film Institute of the Association of American Medical Colleges in formulating methods of production of films that are useful in the classroom and in the development of better ways to utilize films to the best advantage. Source files are maintained by the Medical Film Institute and by the American Medical Association, and teachers are urged to acquire and show to their students a series of selected and recommended films. Sometime in the future we will know better than we can now realize the full value of audiovisual aids in medical teaching. Our most pressing need is more well-made films on anatomy, embryology, physiology, neurology, familial disabilities, chronic systemic diseases, and surgical anatomy. Only through a wide use of pictures in the classroom will we gain the experience to direct the making of better aids.

Attention should be directed to the most useful length of film — one, five, fifteen, thirty minutes or longer, the black and white versus the color film, the addition of sound, and the advisability of dividing the longer film into sections. As means of instruction, audiovisual aids are expensive, so every effort should be made to get the most out of them.

HOME STUDY COURSES

The twelfth annual Home Study Courses in Ophthalmology and Otolaryngology will begin in September and continue through June. On September 1 a new group of approximately five hundred students will begin a systematic review of the basic subjects most closely related to the clinical aspects of these specialties. At the first of each of the ten months the enrollees will receive a list of selected readings in texts and current journals, and in teachers' manuals and supplements available through the Academy Secretary-Treasurer.

The month's reading on one subject, such as Pharmacology and Therapeutics (Swan and Kreft), serves as a refresher course for one who already is familiar with the topics from undergraduate medical school.

The three or four years of internship and residency usually are devoted to clinical experience and to clinical research. Opportunities for laboratory research supported by grants-in-aid from various sources may be provided in some hospitals. Stimulating clinical research may be carried on in any hospital clinic that maintains a teaching staff and adequate records. The Home Study Courses to date have not been extended to cover thoroughly all of the clinical subjects, but the lessons on Refraction, Perimetry, Ocular Motility, External Diseases of the Eye, and, to a limited extent, Ophthalmoscopy afford pertinent reading on clinical aspects of the practice.

All clinics and hospitals which are recommended for residencies in ophthalmology and otolaryngology provide textbooks and current journals suggested by the Home Study Courses faculty, so that the residents in hospitals with a small faculty have access to the latest knowledge on basic subjects and can carry on systematic reading instead of browsing. The reading is directed by

outstanding teachers, who make up the bibliographical references.

Questions relating to the subject under consideration are sent to the subscribers at the end of each month. The answers are reviewed and the papers graded by the Home Study Courses faculty. This procedure is tantamount to a written examination, but for no other purpose than to encourage the enrollee to delve thoroughly into the subject and to obtain an appraisal of his ability. The busy doctor appreciates the value of a course of directed reading on basic subjects, for only by careful, systematic review can he keep abreast of progress in medical practice. The resident requires a quick and thorough review in partial preparation for the Board examinations. The Home Study Courses are designed to fulfill the requirements of both groups, and the time spent in the courses brings rich rewards. The Boards of Examiners recommend them.

FINANCIAL REPORT

Annual Audit for Calendar Year — 1950

May 1, 1951

The American Academy of
Ophthalmology and Otolaryngology
Rochester, Minnesota

Gentlemen:

As requested, we have examined the balance sheet of the American Academy of Ophthalmology and Otolaryngology, an unincorporated association, Rochester, Minnesota, for the year ended December 31, 1950, and the related statements of operations and net worth for the year then ended. Our examination was made in accordance with generally accepted auditing standards, and accordingly included such tests of the accounting records and such other auditing procedures as we deemed necessary in the circumstances. We submit herewith our report which includes the following statements:

Exhibit

"A"—Balance Sheet, December 31, 1950
"B"—Statement of Operations, Year Ended December 31, 1950
"C"—Analysis of Undisbursed Funds from Special Contributions
"D"—Analysis of Net Worth Account
"E"—Analysis of Increase in Market Value of Securities

Schedule

1—Securities Owned, December 31, 1950

Current Assets

Cash on deposit at the various banks was verified by communicating with the depositories, the funds in the Canadian bank being stated in U. S. dollars. The petty cash fund was verified by actual count.

Membership dues receivable, amounting to $878.00, consist of delinquent dues for 1950 and prior years which were verified from the records only. Other receivables totaling $1,753.25 consist of $1,720.00 due from members and others for embryology film, etc., and $33.25 representing various checks held for collection. Inventory of abstracts, manuals, monographs and bound volumes in the amount of $10,310.08 consists of medical publications still on hand December 31, 1950, per inventory records which were accepted without further verification except as to tests of prices, extensions and footings.

Investments

Investments in bonds and stocks, which are described in Schedule No. 1, had a market value of $240,089.63 on December 31, 1950, as compared to $241,447.95 on December 31, 1949. You will observe that U. S. Savings Series "G" bonds are stated at maturity values rather than current redemption prices.

Securities in the "Education Fund," formerly called the "Research Fund," which are held for safekeeping by the Trust Department of the First National Bank, Minneapolis, Minnesota, were verified by communicating with the custodian of the securities. U. S. Savings Series "G" bonds in the "Wherry Memorial Lecture Fund" are held by Dr. W. L. Benedict, Executive Secretary-Treasurer, and were inspected by us. Interest earned on bonds since the dates on which last payments became due, has not been accrued. An analysis of the increase in the market value during the year is shown in Exhibit "E."

Fixed Assets

Furniture, fixtures and equipment amounting to $6,817.69 represent equipment acquired by the Academy over a period of years. Equipment purchased since September 1, 1942, amounting to $5,397.41, was for the most part verified through an inspection of supporting vouchers, and of the latter amount, $387.90 was purchased during the current year. Equipment acquired in years prior to September 1, 1942, which had been charged to operating expenses as purchased, was inventoried and appraised at a market value of $1,420.28 as of January 1, 1944, and set up on the books for that amount. Depreciation has been deducted and charged to operations at a rate that appears to be adequate.

The medical motion picture film, "Embryology of the Eye," was completed during the current year by Sturgis-Grant Productions, Inc., at a total cost of $38,100.00. The master film is being used to produce prints and these are sold to those requesting them. The cost of the original film is being amortized at a rate that appears to be adequate.

Deferred Charges

Unexpired insurance premiums as computed by us amounted to $169.24. Prepaid postage deposit of $161.95, as determined from the records, represents the balance of cash advanced to the U. S. Post Office at Omaha, Nebraska, to be applied as postage on subsequent mailings of the TRANSACTIONS and other publications by the publisher at Omaha. Prepaid interest of $9.45 represents accrued interest on securities purchased by the custodian of the Academy investment portfolio.

Current Liabilities

Accrued expenses totaling $9,340.47 represent unpaid December printing costs of the TRANSACTIONS and other expenses. Membership dues paid in advance totaling $203.00 represent the unearned portion of dues paid for several years in advance by association members.

Undisbursed Funds From Special Contributions

Undisbursed funds from contributions received and designated for "Specific Projects" totaling $11,690.23 are analyzed in Exhibit "C," which shows 1950 transactions as well as prior year balances transferred from net worth account.

Net Worth

An analysis of the net worth of the Academy is shown in Exhibit "D," which reflects an increase from $278,916.22 on December 31, 1949, to $296,038.59 on December 31, 1950.

OPERATIONS

A statement of operations for the year ended December 31, 1950, is presented in Exhibit "B." A summary of this statement and a comparison with the results for the year 1949 is as follows:

	Year 1950	*Year* 1949	*Increase* **Decrease**
Revenues	$158,407.74	$150,545.04	$ 7,862.70
Operating Expenses	137,623.37	123,664.08	13,959.29
Net Income	$ 20,784.37	$ 26,880.96	$ **6,096.59**

The decrease in net income from a year ago is due principally to increased general administrative expenses and increased cost of publishing the TRANSACTIONS.

GENERAL

Upon examination of the insurance policies in force, we found Comprehensive General Liability insurance in the amount of $25,000.00 for each accident, with a total limit of $25,000.00. Workmen's compensation insurance, which is being carried at the statutory amounts, now includes coverage for all persons employed at your annual convention.

The Executive Secretary-Treasurer and Chairman of the Finance Committee are bonded for $25,000.00 each. The principal office employees are bonded for only $1,000.00 each, which in our opinion is inadequate.

Fire and extended coverage on furniture, fixtures and equipment was increased from $6,000.00 to $7,500.00 since the first of the year. Paper stock and publications in custody of the publisher at Omaha, Nebraska, are in-

sured for $12,000.00. Office cash and securities are covered up to $2,400.00 within the premises and $2,100.00 outside the premises against safe burglary and messenger robbery. In view of the considerably larger sums of cash and securities handled by employees, we believe that this coverage should be increased.

We acknowledge the very courteous assistance extended to us by Dr. W. L. Benedict, Executive Secretary-Treasurer of the Academy, and his staff during the progress of this examination.

OPINION

In our opinion, subject to the comments in the preceding paragraphs, the accompanying balance sheet and related statements of operations and net worth present fairly the financial position of The American Academy of Ophthalmology and Otolaryngology at December 31, 1950, and the results of its operations for the year then ended, in conformity with generally accepted accounting principles applied on a basis consistent with that of the preceding year. Respectfully submitted,

BYERS, WOBSCHALL & MILLER
By Edw. A. Wobschall, C.P.A.

EXHIBIT "A"

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
Balance Sheet as at December 31, 1950

ASSETS

Current Assets:			
Cash, First National Bank, Rochester, Minnesota		$ 1,075.89	
Cash, First National bank, Minneapolis, Minnesota		24,644.84	
Cash, Bank of Montreal, Toronto, Canada		676.03	
Petty cash fund		6.00	
Membership dues receivable, delinquent		878.00	
Accounts receivable, other		1,753.25	
Inventory: Abstracts, Manuals, Monographs, etc.		10,310.08	
Total Current Assets			$ 39,344.09
Investments: (Schedule No. 1)			
Bonds and stocks			240,089.63
Fixed Assets:			
Furniture and fixtures	$ 6,817.69		
Less: reserve for depreciation	3,609.76	3,207.93	
Embryology Motion Picture Film	38,100.00		
Less: reserve for depreciation	3,810.00	34,290.00	37,497.93
Deferred Charges:			
Prepaid insurance		169.24	
Prepaid postage deposit		161.95	
Prepaid interest		9.45	340.64
Total Assets			$317,272.29

LIABILITIES AND NET WORTH

Current Liabilities:			
Accrued expenses		$ 9,340.47	
Deferred income, membership dues		203.00	$ 9,543.47
Undisbursed Funds From Special Contributions (Exhibit "C")			
Wherry Memorial Lecture Fund		4,897.72	
Economic Survey of Impaired Hearing		6,200.00	
Sub-committee on Noise in Industry		567.51	
Isabella Wilson Research & Education Fund		25.00	11,690.23
Net Worth (Exhibit "D")			296,038.59
Total Liabilities and Net Worth (*)			$317,272.29

* Subject to report comments.

EXHIBIT "B"

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Statement of Operations

Year Ended December 31, 1950

Revenues:			
Membership dues			$ 27,586.00
Membership applications			5,196.00
Abstracts, manuals and monographs			8,526.08
Certificates			1,030.00
TRANSACTIONS			38,144.80
Home Study Courses			3,612.00
Convention			62,065.50
Testing and calibration of tonometers			1,600.00
Sale of "Embryology of the Eye" film prints			1,675.00
Income from securities:			
Interest, Educational Fund		$ 7,125.00	
Dividends, Educational Fund		1,834.26	
Total			8,959.26
Sundry income			13.10
Total Revenues			158,407.74
Operating Expenses:			
General Administrative		45,069.33	
TRANSACTIONS		43,063.63	
Home Study Courses		7,207.03	
Convention expenses		36,803.38	
Education Fund:			
Supplements, etc.	$ 1,670.00		
Depreciation, Embryology Film	3,810.00	5,480.00	
Total Operating Expenses			137,623.37
Net Income			$ 20,784.37

EXHIBIT "C"

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Analysis of Undisbursed Funds From Special Contributions

WHERRY MEMORIAL LECTURE FUND		
Receipts:		
Interest received on U.S. Savings bonds, year 1950		$ 115.00
Transferred from net worth account:		
Contributions received in prior years		4,600.00
Excess of interest income over expenditures made in prior years		182.72
Balance, December 31, 1950		$ 4,897.72
ECONOMIC SURVEY OF IMPAIRED HEARING FUND		
Receipts:		
Contributions received in 1950		$ 6,200.00
Less: Disbursements		None
Balance, December 31, 1950		$ 6,200.00
SUB-COMMITTEE ON NOISE IN INDUSTRY FUND		
Receipts:		
Contributions received in 1950		$ 6,500.00
Less: Expenditures during 1950	$ 5,840.95	
Excess of 1949 expenditures over receipts transferred from net worth account	91.54	5,932.49
Balance, December 31, 1950		$ 567.51

ISABELLA WILSON RESEARCH & EDUCATION FUND

Receipts:	
Contributions received in 1950	$ 150.00
Less: Expenditures during 1950	125.00
Balance, December 31, 1950	$ 25.00

EXHIBIT "D"

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Analysis of Net Worth Account

For Year Ended December 31, 1950

Net Worth, December 31, 1949		$278,916.22
Additions:		
Net income, year ended December 31, 1950 (Exhibit "B")	$20,784.37	
Increase in market value of securities during 1950 (Exhibit "E")	1,029.18	
Transferred from Sub-committee on Noise in Industry Fund:		
1949 expenditures in excess of receipts	91.54	21,905.09
Total		300,821.31
Deductions:		
Transferred to Wherry Memorial Lecture Fund:		
Contributions received in prior years	4,600.00	
Excess of interest on bonds in Wherry Memorial Lecture Fund over expenditures made in prior years	182.72	4,782.72
Net Worth, December 31, 1950		$296,038.59

EXHIBIT "E"

Analysis of Increase in Market Value of Securities

	Cost	*Market Value*	*Increase* **Decrease**
December 31, 1949	$243,838.48	$241,447.95	**$2,390.53**
December 31, 1950	241,450.98	240,089.63	**1,361.35**
Difference	**$ 2,387.50**	**$1,358.32**	$1,029.18

SCHEDULE No. 1

American Academy of Ophthalmology and Otolaryngology

Securities Owned, December 31, 1950

EDUCATION FUND BONDS	RATE %	MATURITY	PAR VALUE	COST	MARKET VALUE *
Citizens Building Co. of Cleveland 1st Leasehold Sinking Fund	6	1/ 1/46	$ 5,000.00	$ 5,000.00 (1)	
Van Swerigen Co. Certificates of Indebtedness, Series 1925	6	12/31/48	6,000.00	3,477.03 (2)	$ 825.00
Dominion of Canada 8th Victory Loan, Ser. P5	3	10/ 1/63	2,500.00	2,500.00 (3)	2,343.75
Dominion of Canada, 8th Victory Loan, Ser. P5	3	10/ 1/63	5,000.00	5,112.50 (3)	4,687.50
U.S.A. Savings, Series F	2½	12/ 1/55	13,500.00	9,990.00	11,448.00
U.S.A. Savings, Series G	2½	8/ 1/53	10,000.00	10,000.00 (4)	10,000.00
U.S.A. Savings, Series G	2½	6/ 1/55	4,000.00	4,000.00 (4)	4,000.00
U.S.A. Savings, Series G	2½	3/ 1/56	6,000.00	6,000.00 (4)	6,000.00
U.S.A. Savings, Series G	2½	5/ 1/56	8,000.00	8,000.00 (4)	8,000.00
U.S.A. Savings, Series G	2½	7/ 1/56	2,000.00	2,000.00 (4)	2,000.00
U.S.A. Savings, Series G	2½	11/ 1/56	25,000.00	25,000.00 (4)	25,000.00
U.S.A. Savings, Series G	2½	1/ 1/57	2,000.00	2,000.00 (4)	2,000.00
U.S.A. Savings, Series G	2½	7/ 1/58	30,000.00	30,000.00 (4)	30,000.00
U.S.A. Savings, Series G	2½	12/ 1/58	25,000.00	25,000.00 (4)	25,000.00
U.S.A. Savings, Series G	2½	3/ 1/59	15,000.00	15,000.00 (4)	15,000.00
U.S.A. Savings, Series G	2½	7/ 1/60	30,000.00	30,000.00 (4)	30,000.00
U.S.A. Treasury, 1967-72	2½	12/15/72	10,000.00	10,000.00	10,068.75
U.S.A. Treasury, 1967-72	2½	12/15/72	15,000.00	15,431.25	15,103.13
Total Bonds				$208,510.78	$201,476.13

STOCKS	KIND	PAR VALUE	SHARES		
Citizens Building Co. of Cleveland	Shares	No Par	50	None	None
Commonwealth Edison Co.	Common	$25.00	100	$ 2,619.00	$ 2,762.50
E. I. duPont de Nemours & Co.	Common	5.00	60	2,347.31	5,040.00
Louisville Gas & Electric Co.	5% Pfd.	25.00	200	5,450.00	5,750.00
Massachusetts Investors Trust	Trust Cert.	1.00	617	17,923.89	20,361.00
Ophthalmic Publishing Co.	Capital	20.00	5	None	100.00
Total Stocks				$ 28,340.20	$ 34,013.50
Total Education Fund				$236,850.98	$235,489.63

WHERRY MEMORIAL LECTURE FUND

	RATE	MATURITY	PAR VALUE		
U.S.A. Savings, Series G	2½	1955	$4,600.00	$ 4,600.00	$ 4,600.00
Total Investments				$241,450.98	$240,089.63

(*) Except for U.S.A. Savings Series G bonds, which are included at maturity values
(1) No market available
(2) Partial liquidation received in 1949
(3) U. S. dollars
(4) Maturity values

SECTION ON INSTRUCTION

FIFTY-SIXTH ANNUAL MEETING

American Academy of Ophthalmology and Otolaryngology

October 14-19, 1951
PALMER HOUSE
Chicago, Illinois

DEAN M. LIERLE, M.D.
Secretary for Instruction — Otolaryngology and Maxillofacial Surgery

A. D. RUEDEMANN, M.D.
Secretary for Instruction — Ophthalmology

The following condensed schedules of instruction courses are reprinted for the convenience of Fellows who have not yet placed orders for tickets.

Courses already sold out are so designated on the charts. Please do not request tickets for these courses.

For complete listing of course titles, instructors, and descriptive paragraphs about each subject, please refer to the March-April issue of the TRANSACTIONS.

General Instructions

Only members who have paid their 1951 *dues may order instruction tickets in advance of the meeting.* Members should order tickets only for their own use. Candidates for fellowship in the Academy are not privileged to reserve tickets in advance. After the session opens, no distinction between members, candidates and guests will be made in selling tickets.

Each period (1 hour) of instruction costs $1.50. *Orders unaccompanied by properly executed checks will not be filled.* Checks should be made payable to W. L. Benedict, M.D.

In case of inability to attend the meeting after order has been filled, a refund will be granted if requested prior to October 12.

If courses requested are not available and it is impossible to substitute, a refund will be granted. Refunds will not be sent by mail. A blue refund card will be placed in the Advance Registration Envelope which is received at the time of registration. This should be presented at the Instruction Desk for payment.

All orders for tickets will be filled according to postmark on envelope containing check. Telegrams will not be honored. Previous to October 1, send orders to 100 First Avenue Building, Rochester, Minnesota; after October 1, mail orders direct to W. L. Benedict, M.D., c/o Palmer House, Chicago, Illinois. Advance orders will not be filled if received after October 12.

Ordering Instruction Tickets

An *individual* course is complete in 1 period. Most individual courses are repeated on two or three different days allowing the subscriber to choose the day on which he wishes to attend.

A *continuous* course lasts 2 or more periods as indicated. It is not possible to purchase a ticket to only *part* of a continuous course.

At the end of this section is printed a colored sheet to be used when ordering tickets in advance. Specify preferences on this sheet and mail to the executive

office. Careful attention to instructions will ensure the correct filling of your requests. *Since number of tickets for each course is limited it is necessary that you select more courses than it is possible for you to attend; in other words, a list of three preferences for each period selected should be given.*

If you are requesting registration in the continuous courses, please specify preferences for individual courses as substitutes in order to avoid disappointment should the continuous courses which you select be sold out when your order is received.

Acknowledgment of Advance Order

As soon as an advance order is filled, a postcard, listing the courses that have been reserved for him, will be mailed to the subscriber. In each case, every effort is made to include first choices. Please do not ask to change courses after your order has been filled. The postcard is merely an assurance that your order has been filled; it is not necessary for registration at the Academy meeting.

Claiming Instruction Tickets

No tickets will be sent through the mails. Members who have ordered instruction course tickets will register at the *Advance Order Section* of the Registration Desk during the week of the Convention to secure registration badge, tickets, and all convention material.

KEY TO DESIGNATION OF PERIODS

The periods will be designated with the following key: Select tickets for —
Otolaryngology, forenoons, periods 1-2-3 — Ophthalmology, afternoons, periods 4-5-6

Day	(M)onday	(T)uesday	(W)ednesday	(Th)ursday
Period a.m.		1 2 3	1 2 3	1 2 3
Period p.m.	4 5 6	4 5 6	4 5 6	4 5 6

M-4	2:00 p.m.	to	3:00 p.m.	W-4	2:00 p.m. to 3:00 p.m.
M-5	3:15 p.m.	to	4:15 p.m.	W-5	3:15 p.m. to 4:15 p.m.
M-6	4:30 p.m.	to	5:30 p.m.	W-6	4:30 p.m. to 5:30 p.m.
T-1	9:00 a.m.	to	10:00 a.m.	Th-1	9:00 a.m. to 10:00 a.m.
T-2	10:15 a.m.	to	11:15 a.m.	Th-2	10:15 a.m. to 11:15 a.m.
T-3	11:30 a.m.	to	12:30 p.m.	Th-3	11:30 a.m. to 12:30 p.m.
T-4	2:00 p.m.	to	3:00 p.m.	Th-4	2:00 p.m. to 3:00 p.m.
T-5	3:15 p.m.	to	4:15 p.m.	Th-5	3:15 p.m. to 4:15 p.m.
T-6	4:30 p.m.	to	5:30 p.m.	Th-6	4:30 p.m. to 5:30 p.m.
W-1	9:00 a.m.	to	10:00 a.m.		
W-2	10:15 a.m.	to	11:15 a.m.		
W-3	11:30 a.m.	to	12:30 p.m.		

(Familiarity with this key will be helpful and will avoid confusion)

CHANGE IN INSTRUCTION COURSE PROGRAM AS LISTED IN THE MARCH-APRIL 1951 TRANSACTIONS

A course in **Anesthesia,** to be given by Dr. John W. Pender, Rochester, Minn. (by invitation), has been added to the Individual Courses in Otolaryngology. As Course 493 it will be presented in Room 712 on Tuesday, period 3, and will be repeated in Room 781 on Wednesday, period 3. The lecture will be illustrated by a motion picture.

CONTINUOUS COURSES — OPHTHALMOLOGY

COURSE	SPEAKERS	SUBJECT	PERIODS USED
1	Adler	Physiology of Vision	3 PERIODS M-6, T-6, W-6
2 or 3	Allen, J. H.	Bacteriology	2 PERIODS M-4, M-5 or T-4, T-5
4	Bedell	Medical Ophthalmoscopy	4 PERIODS M-4, T-4, W-4, Th-4
5	Berliner	Slit Lamp Microscopy	4 PERIODS M-5, T-5, W-5, Th-5
6 or 7	Boeder	Aniseikonia & Space Eikonometry	2 PERIODS M-4, M-5 or T-4, T-5
8	Brown, et al	Eye Muscles	8 PERIODS M-4, M-5, T-4, T-5, W-4, W-5, Th-4, Th-5
9 or 10	Copeland	Streak Retinoscopy	4 PERIODS M-4, M-5, T-4, T-5 or W-4, W-5, Th-4, Th-5
11	Costenbader, et al	Concomitant Strabismus	12 PERIODS M-4, M-5, M-6, T-4, T-5, T-6, W-4, W-5, W-6, Th-4, Th-5, Th-6
12	Dunnington & Wheeler	Heterophoria & Heterotropia	6 PERIODS M-4, M-5, T-4, T-5, W-4, W-5
13	Fralick	Applied Anatomy	4 PERIODS M-4, T-4, W-4, Th-4
14	Gordon	Perimetry	4 PERIODS M-6, T-6, W-6, Th-6
15	Haas & McGarry	Introduction to Gonioscopy	2 PERIODS W-5, W-6
16	Hardy, et al	Basic Principles of Orthoptics	4 PERIODS M-6, T-6, W-6, Th-6
17	Hastings	Psychosomatic Medicine	2 PERIODS W-4, W-5
18	Henderson	Neurologic Applied Anatomy	3 PERIODS M-6, T-6, W-6
19	Hughes, et al	Plastic Surgery	8 PERIODS M-5, M-6, T-5, T-6 W-5, W-6, Th-5, Th-6
20	Jardon	Fitting of Ocular Prostheses	2 PERIODS M-4, M-5
21	Knighton, et al	Highlights of Glaucoma	6 PERIODS M-4, M-5, T-4, T-5, W-4, W-5
22	Kuhn	Industrial Ophthalmology	3 PERIODS M-4, T-4, W-4
23	Lloyd	Corneal Lesions	2 PERIODS M-4, M-5
24	McLean, et al	Cataract Surgery	12 PERIODS M-4, M-5, M-6, T-4, T-5, T-6, W-4, W-5, W-6, Th-4, Th-5, Th-6
25	Meyer, et al	Glaucoma	8 PERIODS M-5, M-6, T-5, T-6, W-5, W-6, Th-5, Th-6
26	Newell	Rabbit Surgery	2 PERIODS Th-4, Th-5

CONTINUOUS COURSES — OPHTHALMOLOGY

COURSE	SPEAKERS	SUBJECT	PERIODS USED
27	Ogle	Problems of Binocular Vision	2 PERIODS M-4, M-5
28	O'Rourke	Manifest & Cycloplegic Refraction	2 PERIODS T-4, T-5
29	Payne, et al	Special Eye Pathology	8 PERIODS M-4, M-5, T-4, T-5, W-4, W-5, Th-4, Th-5
30	Regan	Refraction	12 PERIODS M-4, M-5, M-6, T-4, T-5, T-6, W-4, W-5, W-6, Th-4, Th-5, Th-6
31 or 32	Rychener	External Diseases of Eye	2 PERIODS M-4, M-5 or T-4, T-5
33	Scarney & Johnson	Slit Lamp Biomicroscopy	8 PERIODS M-5, M-6, T-5, T-6 W-5, W-6, Th-5, Th-6
34	Scobee, et al	Oculorotary Muscles	12 PERIODS M-4, M-5, M-6, T-4, T-5, T-6, W-4, W-5, W-6, Th-4, Th-5, Th-6
35	Simpson	Office Management of Phorias	2 PERIODS T-4, T-5
36	Stow, et al	Clinical Pathology	8 PERIODS M-5, M-6, T-5, T-6, W-5, W-6, Th-5, Th-6
37	Theobald, et al	Histopathology	12 PERIODS M-4, M-5, M-6, T-4, T-5, T-6, W-4, W-5, W-6, Th-4, Th-5, Th-6
38	Thorpe, et al	Slit Lamp Biomicroscopy	12 PERIODS M-4, M-5, M-6, T-4, T-5, T-6, W-4, W-5, W-6, Th-4, Th-5, Th-6
39	Vail & Minsky	Operation of Choice in Cataract Surgery	2 PERIODS Th-4, Th-5
40	Wiener	Practical Points in Surgery	3 PERIODS T-4, W-4, Th-4
41	Falls	Value of Film on Embryology	2 PERIODS W-5, W-6

SCHEDULE OF INDIVIDUAL COURSES — OPHTHALMOLOGY — Monday

Key M-4 — 2:00 p.m. to 3:00 p.m.

Course No.	SPEAKER	SUBJECT
205	Atkinson	Measures in Cataract Extraction
212	Burian	Neuromuscular Anomalies: Surgical Treatment
215	Calhoun	Dystrophies & Degenerations of Cornea
233	Egan	Cross Cylinder Application & Theory
234	Elwyn	Fundus Changes in Arterial Hypertension
241	Fread	Ideal Refraction Equipment
243	Gemeroy	External Diseases of Eye
255	Jobe	Practical Physiologic Optics
260	Kornzweig	Embryologic Basis for Developmental Anomalies
274	Mann, W.	Refraction & Lens for Cataract Patient
280	Owens & Owens	Retrolental Fibroplasia
282	Perera	End Results in Retinal Detachment
313	Woods	ACTH & Cortisone
314	Yudkin	Deficiency Diseases
A	Home Study	Anatomy & Embryology

Key M-5 — 3:15 p.m. to 4:15 p.m.

Course No.	SPEAKER	SUBJECT
202	Alvaro	Uveitis
208	Bedell	Unusual Fundus Lesions
216	Callahan	Repair of Lid Lacerations
226	Culler	Chiasmal Syndromes
229	Davies	Clinical Pathology in Optic Atrophy
237	Falls	Ocular Geriatrics
242	Gailey	Type of Surgery for Cataract Patient
245	Gipner	Recent Advances
252	Hitz	Headaches in Children: Etiology
253	Iliff	Beta Irradiation Therapy
273	Mann, M.	Hypertensive Changes in Fundus
299	Stine	Retinal Detachment
311	Whalman	Surgical Procedures
B	Home Study	Physiology

Key M-6 — 4:30 p.m. to 5:30 p.m.

Course No.	SPEAKER	SUBJECT
203	Alvis	End Results of Cataract Wound Closures
206	Baird	Acute Lesions of Cornea
210	Bettman	Orbital Lesions
211	Braley	Virus Diseases
221	Clark	Indications & Uses for Iridectomy
225	Cruthirds	Burns of Eye
230	DeVoe	Clinical Application of Gonioscopy
231	Dunlap	Divergence Anomalies
239	Finegan	Ocular Tuberculosis
247	Gray	Intraocular Foreign Bodies
248	Guibor	Physiology of Ocular Muscles
254	Irvine	Uveitis
257	Kirby	Problems of Cataract Surgery
268	Lepard	Eye Diseases Common to Children
275	Marshall	Chronic Infections of Lid
281	Paton	Corneal Surgery
287	Posner	Secondary Glaucoma
293	Scheie	Surgery in Congenital Glaucoma
297	Spaeth	Lacrimal Gland & Sac
C	Home Study	Optics & Visual Physiology

SCHEDULE OF INDIVIDUAL COURSES — OPHTHALMOLOGY — Tuesday

Key T-4 — 2:00 p.m. to 3:00 p.m.

Course No.	SPEAKER	SUBJECT
205	Atkinson	Measures in Cataract Extraction
207	Baker	Neuralgias of Head
209	Berens	Highlights of Ophthalmic Surgery
215	Calhoun	Dystrophies & Degenerations of Cornea
217	Carter	Vascular Diseases of Fundus
227	Cusick	Ptosis
233	Egan	Cross Cylinder Application & Theory
235	Elwyn	Heredodegenerative Diseases of Retina
241	Fread	Ideal Refraction Equipment
243	Gemeroy	External Diseases of Eye
255	Jobe	Practical Physiologic Optics
274	Mann, W.	Refraction & Lens for Cataract Patient
280	Owens & Owens	Retrolental Fibroplasia
282	Perera	End Results in Retinal Detachment
314	Yudkin	Deficiency Diseases
D	Home Study	Refraction

Key T-5 — 3:15 p.m. to 4:15 p.m.

Course No.	SPEAKER	SUBJECT
202	Alvaro	Uveitis
214	Byrnes	Adjuncts in Teaching Ophthalmology
216	Callahan	Repair of Lid Lacerations
220	Chandler	Secondary Glaucoma
226	Culler	Chiasmal Syndromes
229	Davies	Clinical Pathology in Optic Atrophy
238	Falls	Practical Application of Heredity
242	Gailey	Type of Surgery for Cataract Patient
245	Gipner	Recent Advances
252	Hitz	Headaches in Children: Etiology
253	Iliff	Beta Irradiation Therapy
273	Mann, M.	Hypertensive Changes in Fundus
288	Post	Problems in Refraction
311	Whalman	Surgical Procedures
E	Home Study	External Diseases of Eye

Key T-6 — 4:30 p.m. to 5:30 p.m.

Course No.	SPEAKER	SUBJECT
203	Alvis	End Results of Cataract Wound Closures
206	Baird	Acute Lesions of Cornea
210	Bettman	Orbital Lesions
211	Braley	Virus Diseases
221	Clark	Indications & Uses for Iridectomy
225	Cruthirds	Burns of Eye
230	DeVoe	Clinical Application of Gonioscopy
231	Dunlap	Divergence Anomalies
239	Finegan	Ocular Tuberculosis
247	Gray	Intraocular Foreign Bodies
249	Guibor	Neuromotor Defects of Ocular Muscles
254	Irvine	Uveitis
261	Krause	Infections of Internal Eye
268	Lepard	Eye Diseases Common to Children
275	Marshall	Chronic Infections of Lid
281	Paton	Corneal Surgery
287	Posner	Secondary Glaucoma
293	Scheie	Surgery in Congenital Glaucoma
297	Spaeth	Lacrimal Gland & Sac
304	Thygeson	Herpetic Viruses
F	Home Study	Perimetry

SCHEDULE OF INDIVIDUAL COURSES — OPHTHALMOLOGY — Wednesday

Key W-4 — 2:00 p.m. to 3:00 p.m.

Course No.	SPEAKER	SUBJECT
207	Baker	Neuralgias of Head
217	Carter	Vascular Diseases of Fundus
222	Cosgrove	Subacute & Chronic Conjunctivitis
223	Cowen	Acute Affections of Orbit
227	Cusick	Ptosis
228	Cutler	Procedures Used in Enucleation
240	Fink	Surgical Anatomy of Oblique Muscles
246	Givner	Systemic Disease
251	Hester	Clinical Photography
263	Lancaster	Tests for Ocular Deviations
265	Lebensohn	Optical Problems of Presbyopia
266	Leinfelder	Papilledema & Optic Neuritis
269	Linksz	Ocular Therapeutics
270	Lueck	Practical Optics
277	McLaughlin	Chemical Eye Injuries
284	Pfeiffer	Diagnosis with Aid of X-ray
290	Reese	Tumors of Eye & Adnexa
291	Rucker	Lesions in Region of Chiasm
301	Swan	Value of Drugs Used in Glaucoma
G	Home Study	Extraocular Muscles

Key W-5 — 3:15 p.m. to 4:15 p.m.

Course No.	SPEAKER	SUBJECT
204	Ascher	Aqueous Veins
218	Cassady	Dacryocystitis of Infancy
219	Chace	Malingering
244	Gifford	Dacryocystorhinostomy
259	Klien	Clinical Pathology of Retinal Lesions
262	Kronfeld	Present Trends in Ophthalmology
264	Leahey	External Ocular Malignancy
267	Lemoine	Vitreous Opacities
272	Mangold	Proper Fitting of Glasses
276	McGuire	Surgery of Vertical Muscles
278	Morrison	Office Management of Glaucoma
279	Mullen	Ophthalmic Emergencies
283	Perritt	Advances in Corneal Surgery
285	Pino	Problems of Bifocal Lenses
292	Rundles	Streak Retinoscopy
299	Stine	Retinal Detachment
305	Town	Fibrin Coagulum in Ocular Surgery
H	Home Study	Ophthalmoscopy & Slit Lamp

Key W-6 — 4:30 p.m. to 5:30 p.m.

Course No.	SPEAKER	SUBJECT
250	Guibor	Neurology of Ocular Muscles
256	Katz	Corneal Dystrophies
258	Kirby	Surgery of Lateral Canthus & Eyelids
271	Macnie	Eye Changes in Head Trauma
294	Schepens	Technic of Indirect Ophthalmoscopy
296	Smith	Practical Points in Office Treatment
300	Sullivan	Practical Perimetry
302	Tait	Accommodation & Convergence Reflexes
303	Tassman	Use of Coagulants in Wound Closure
304	Thygeson	Herpetic Viruses
306	Trueman	Demyelinizing Diseases
307	Vail	Cataract Extraction by Smith Method
308	Veasey	Refraction Difficulties
309	von Sallmann	Antibiotics
310	Weisser	The Traumatic Eye
312	Wood	Earliest Diagnosis of Macular Lesions
I	Home Study	Pathology

SCHEDULE OF INDIVIDUAL COURSES — OPHTHALMOLOGY — Thursday

Key Th-4 — 2:00 p.m. to 3:00 p.m.

Course No.	SPEAKER	SUBJECT
201	Allen, T.	Office Practice
213	Burian	Neuromuscular Anomalies: Nonsurgical Treatment
222	Cosgrove	Subacute & Chronic Conjunctivitis
223	Cowen	Acute Affections of Orbit
232	Dunnington	End Results in Muscle Surgery
240	Fink	Surgical Anatomy of Oblique Muscles
246	Givner	Systemic Disease
251	Hester	Clinical Photography
263	Lancaster	Tests for Ocular Deviations
265	Lebensohn	Optical Problems of Presbyopia
266	Leinfelder	Papilledema & Optic Neuritis
269	Linksz	Ocular Therapeutics
270	Lueck	Practical Optics
277	McLaughlin	Chemical Eye Injuries
284	Pfeiffer	Diagnosis with Aid of X-ray
289	Randolph	Handling of Patients with Advanced Glaucoma
291	Rucker	Lesions in Region of Chiasm
295	Siniscal	Chronic Lid Conditions
298	Spaeth	Plastic Surgery
J	Home Study	Pharmacology & Therapeutics

Key Th-5 — 3:15 p.m. to 4:15 p.m.

Course No.	SPEAKER	SUBJECT
218	Cassady	Dacryocystitis of Infancy
219	Chace	Malingering
244	Gifford	Dacryocystorhinostomy
259	Klien	Clinical Pathology of Retinal Lesions
264	Leahey	External Ocular Malignancy
267	Lemoine	Vitreous Opacities
272	Mangold	Proper Fitting of Glasses
276	McGuire	Surgery of Vertical Muscles
278	Morrison	Office Management of Glaucoma
279	Mullen	Ophthalmic Emergencies
283	Perritt	Advances in Corneal Surgery
286	Pino	Lenses for Difficult Prescription
292	Rundles	Streak Retinoscopy
305	Town	Fibrin Coagulum in Ocular Surgery

Key Th-6 — 4:30 p.m. to 5:30 p.m.

Course No.	SPEAKER	SUBJECT
294	Schepens	Technic of Indirect Ophthalmoscopy
300	Sullivan	Practical Perimetry
302	Tait	Accommodation & Convergence Reflexes
306	Trueman	Demyelinizing Diseases
307	Vail	Cataract Extraction by Smith Method
308	Veasey	Refraction Difficulties
309	von Sallmann	Antibiotics
312	Wood	Earliest Diagnosis of Macular Lesions

CONTINUOUS COURSES — OTOLARYNGOLOGY

COURSE	SPEAKERS	TITLE	PERIODS USED
101	Altman & Waltner	Histopathology of Ear—Part I	2 PERIODS T-1, T-2
102	Altman & Waltner	Histopathology of Ear—Part II	2 PERIODS W-1, W-2
103 or 104	Converse	Nasal Plastic Surgery	2 PERIODS T-1, T-2 or W-1, W-2
105 or 106	Figi	Lesions of Mouth	2 PERIODS T-2, T-3 or W-2, W-3
107	Fowler & Montreuil	Histology of Ear—Vertical Sections	2 PERIODS T-2, T-3
108	Fowler & Montreuil	Histology of Ear—Horizontal Sections	2 PERIODS W-2, W-3
109 or 110 or 111	Hansel	Allergy	2 PERIODS T-1, T-2 or W-1, W-2 or Th-1, Th-2
112	Jackson	Technic in Peroral Endoscopy	3 PERIODS T-1, W-2, Th-3
113	Kazanjian, et al	Traumatic Injuries of Face	2 PERIODS Th-1, Th-2
114 or 115 or 116	Lempert	Modern Temporal Bone Surgery	2 PERIODS T-2, T-3 or W-2, W-3 or Th-2, Th-3
117 or 118	Lindsay	Vertigo	2 PERIODS W-2, W-3 or Th-2, Th-3
119	Marcus, et al	Hearing Problems in Children	2 PERIODS T-2, T-3
120 or 121	Martin	Cancer of Larynx	2 PERIODS T-1, T-2 or W-1, W-2
122 or 123	Moses	Speech & Voice Therapy	2 PERIODS T-1, T-2 or W-1, W-2
124 or 125	Mueller	Practical Audiometry	2 PERIODS W-2, W-3 or Th-2, Th-3
126 or 127	Orton	Applied Surgery of Neck	2 PERIODS T-1, T-2 or W-1, W-2
128	Owen	Attic-Aditus-Antrum Area	2 PERIODS T-1, T-2
129	Tucker, et al	Esophageal Disease & Foreign Bodies	3 PERIODS T-1, W-1, Th-1
130	Tucker, et al	Laryngeal Surgery	3 PERIODS T-2, W-2, Th-2
131 or 132	Turchik	Rhinoplasty	2 PERIODS W-2, W-3 or Th-2, Th-3

SCHEDULE OF INDIVIDUAL COURSES — OTOLARYNGOLOGY — Tuesday

Key T-1 — 9:00 a.m. to 10:00 a.m.

Course No.	SPEAKER	SUBJECT
401	Alexander	Deafness
402	Anthony & Fisher	The Fractured Orbit
403	Ashley	Dust Therapy in Respiratory Allergy
411	Boxer	Endoscopic Problems in Children
416	Costen	Mandibular Joint Syndrome
419	Day	What the Otologist Can Do for Deafness
428	Goodhill	Management of Tinnitus
429	Gundrum	Secretions of ENT: Cytologic Study
435	Holinger	Diseases of Esophagus
438	Holmes	Scars of the Face
444	Keaster	Speech & Hearing in Children Under Five
445	Kemler	Laryngeal Lesions
455	McLaurin	Chronic External Otitis
459	Morrison	Technic of Tonsillectomy
461	Ogura	One-Stage Widefield Laryngectomy
463	Persky	Acute & Chronic Suppurative Otitis Media
468	Roberts, S. E.	Headache
470	Sataloff	Present Treatment of Nerve Deafness
474	Shambaugh	Allergy in Relation to Sinusitis
480	Spector	Autonomic Nervous System
484	Teed	Temporal Bone—Vertical Sections
487	Von Leden	Tracheotomy
N	Home Study	Vestibular Function & Testing

Key T-2 — 10:15 a.m. to 11:15 a.m.

Course No.	SPEAKER	SUBJECT
417	Craft	Nasal Surgery in Allergic Patient
423	Erich	Malignant Lesions of Face
425	Forman	Problems in Laryngoscopy
437	Hollender	Sore Throat
441	Johnson	Stuttering
447	Kuhn	Allergic Diseases of Ear
452	Macgregor	Sociologic & Psychologic Aspects of Nasal Deformities
453	Maliniac	Sequelae in Corrective Rhinoplasty
458	Moore	Cysts & Fistulas of Face & Neck
462	Perlman	Deafness as Related to Eustachian Tube Disease
467	Roberts, G.J.	Management of Nasal Fractures
473	Senturia	Treatment of External Otitis
476	Simonton	Recruitment of Loudness & Diplacusis Binauralis
478	Slaughter	Recent & Old Fractures of Facial Bones
481	Spector	Dynamics of Neural Pathways in Vertigo
488	Walsh	Vasomotor Rhinitis & Chronic Sinusitis
O	Home Study	Histology

Key T-3 — 11:30 a.m. to 12:30 p.m.

Course No.	SPEAKER	SUBJECT
409	Becker	Plastic Surgery of Protruding Ears
415	Converse	Corrective Surgery of Nasal Deviations
420	Derlacki & Shambaugh	Skin Testing in Nasal Allergy
421	DeWeese	The Dizzy Patient
427	Goldman	Clinical Bacteriology
443	Juers	Hearing Tests
448	Landis	Hearing Testing Programs in Public Schools
449	Lederer	Kodachrome Clinic
451	Lynch	Technic of Intralaryngeal Surgery
454	Maxwell	Facial Paralysis
456	McNally	Labyrinthine Tests
464	Putney	Surgery of Neck Tumors
466	Richards	Suggestions Concerning Office Practice
469	Robison	Management of Allergic Sinusitis
471	Sellers	Chronically Infected Ear
472	Seltzer	Plastic Surgery of Nose
483	Sullivan	Surgical Treatment of Facial Paralysis
489	Wilkerson	Hearing & Speech Center for Your City
493	Pender	Anesthesia
P	Home Study	Pathology

SCHEDULE OF INDIVIDUAL COURSES — OTOLARYNGOLOGY — Wednesday

Key W-1 — 9:00 a.m. to 10:00 a.m.

Course No.	SPEAKER	SUBJECT
401	Alexander	Deafness
403	Ashley	Dust Therapy in Respiratory Allergy
405	Barone	Hay Fever
406	Batson	Anatomy of Ear
410	Boies	Headaches & Neuralgia of Nasal Origin
411	Boxer	Endoscopic Problems in Children
412	Carhart	The Audiogram in Otologic Diagnosis
416	Costen	Mandibular Joint Syndrome
419	Day	What the Otologist Can Do for Deafness
424	Farrior	Primary Skin Graft in Radical Mastoidectomy
429	Gundrum	Secretions of ENT: Cytologic Study
432	Hilger	Autonomic Dysfunction
433	Hill	Mistakes Made in Otolaryngology
435	Holinger	Diseases of Esophagus
438	Holmes	Scars of the Face
439	House	Surgery of Chronically Discharging Ear
445	Kemler	Laryngeal Lesions
452	Macgregor	Sociologic & Psychologic Aspects of Nasal Deformities
455	McLaurin	Chronic External Otitis
463	Persky	Acute & Chronic Suppurative Otitis Media
477	Singleton	Catarrhal Otitis Media with Effusion
482	Spector	Interpretative Anatomy of Trigeminal Neuralgia, etc.
484	Teed	Temporal Bone—Vertical Sections
492	Wright	Topical Antiseptics & Antibiotics—Pharmacology
Q	Home Study	Hearing Function & Testing

Key W-2 — 10:15 a.m. to 11:15 a.m.

Course No.	SPEAKER	SUBJECT
402	Anthony & Fisher	The Fractured Orbit
407	Batson	Anatomy of Nose
417	Craft	Nasal Surgery in Allergic Patient
422	Equen	Magnetic Removal of Foreign Bodies
423	Erich	Malignant Lesions of Face
425	Forman	Problems in Laryngoscopy
426	Furstenberg	Tumors & Cysts of Head & Neck of Teratologic Origin
430	Harkness	Signs, Syndromes, & Triads in Private Practice
437	Hollender	Sore Throat
440	Hunnicutt	Chronically Congested Nose
441	Johnson	Stuttering
447	Kuhn	Allergic Diseases of Ear
465	Rawlins	Mechanisms in Allergy in Relation to ENT Conditions
475	Shuster	Cranial Nerves
476	Simonton	Recruitment of Loudness & Diplacusis Binauralis
479	Spar	Control of Nasal Hemorrhage
486	Thornell	Intralaryngeal Arytenoidectomy
490	Williams	Specific Medical Treatment of Allergies
R	Home Study	Pharmacology

Key W-3 — 11:30 a.m. to 12:30 a.m.

Course	SPEAKER	SUBJECT
404	Baron	Modified Radical Mastoidectomy
408	Batson	Anatomy of Larynx & Neck
409	Becker	Plastic Surgery of Protruding Ears
413	Cohen	Deviated Noses
415	Converse	Corrective Surgery of Nasal Deviations
418	Davison	Bronchopulmonary Infections in Allergic Individuals
420	Derlacki & Shambaugh	Skin Testing in Nasal Allergy
421	DeWeese	The Dizzy Patient
427	Goldman	Clinical Bacteriology
428	Goodhill	Management of Tinnitus
431	Hesser	Facial & Other Head Pain
434	Holinger	Bronchoscopic Technics
436	Hollander	Problems in Use of Cortisone & ACTH
442	Jones	Management of Ear Problems in Children
443	Juers	Hearing Tests
446	Kinney	Hearing Conservation in Children
448	Landis	Hearing Testing Programs in Public Schools
449	Lederer	Kodachrome Clinic
450	Long	Chemotherapeutic & Antibiotic Agents
457	Miller	Laryngeal Emergencies in Infants & Children
460	Myklebust	Deafness in Young Children
469	Robison	Management of Allergic Sinusitis
480	Spector	Autonomic Nervous System
485	Teed	Temporal Bone—Horizontal Sections
491	Work	Technic of Endaural Incisions
493	Pender	Anesthesia
S	Home Study	Physiology

SCHEDULE OF INDIVIDUAL COURSES — OTOLARYNGOLOGY — Thursday

Key Th-1 — 9:00 a.m. to 10:00 a.m.

Course No.	SPEAKER	SUBJECT
405	Barona	Hay Fever
406	Batson	Anatomy of Ear
410	Boies	Headaches & Neuralgia of Nasal Origin
412	Carhart	The Audiogram in Otologic Diagnosis
424	Farrior	Primary Skin Graft in Radical Mastoidectomy
432	Hilger	Autonomic Dysfunction
433	Hill	Mistakes Made in Otolaryngology
439	House	Surgery of Chronically Discharging Ear
442	Jones	Management of Ear Problems in Children
444	Keaster	Speech & Hearing in in Children Under Five
451	Lynch	Technic of Intralaryngeal Surgery
454	Maxwell	Facial Paralysis
459	Morrison	Technic of Tonsillectomy
461	Ogura	One-Stage Widefield Laryngectomy
468	Roberts, S. E.	Headache
470	Sataloff	Present Treatment of Nerve Deafness
474	Shambaugh	Allergy in Relation to Sinusitis
477	Singleton	Catarrhal Otitis Media with Effusion
481	Spector	Dynamics of Neural Pathways in Vertigo
483	Sullivan	Surgical Treatment of Facial Paralysis
487	Von Leden	Tracheotomy
492	Wright	Topical Antiseptics & Antibiotics—Pharmacology
T	Home Study	Bacteriology

Key Th-2 — 10:15 a.m. to 11:15 a.m.

Course No.	SPEAKER	SUBJECT
407	Batson	Anatomy of Nose
414	Conn	Clinical Aspects of ACTH & Cortisone
422	Equen	Magnetic Removal of Foreign Bodies
426	Furstenberg	Tumors & Cysts of Head & Neck of Teratologic Origin
430	Harkness	Signs, Snydromes, & Triads in Private Practice
440	Hunnicutt	Chronically Congested Nose
453	Maliniac	Sequelae in Corrective Rhinoplasty
458	Moore	Cysts & Fistulas of Face & Neck
462	Perlman	Deafness as Related to Eustachian Tube Disease
464	Putney	Surgery of Neck Tumors
465	Rawlins	Mechanisms in Allergy in Relation to ENT Conditions
467	Roberts, G. J.	Management of Nasal Fractures
473	Senturia	Treatment of External Otitis
475	Shuster	Cranial Nerves
478	Slaughter	Recent & Old Fractures of Facial Bones
482	Spector	Interpretative Anatomy of Trigeminal Neuralgia, etc.
486	Thornell	Intralaryngeal Arytenoidectomy
488	Walsh	Vasomotor Rhinitis & Chronic Sinusitis
490	Williams	Specific Medical Treatment of Allergies
U	Home Study	Applied Anatomy in Otolaryngology

Key Th-3 — 11:30 a.m. to 12:30 p.m.

Course No.	SPEAKER	SUBJECT
404	Baron	Modified Radical Mastoidectomy
408	Batson	Anatomy of Larynx & Neck
413	Cohen	Deviated Noses
414	Conn	Clinical Aspects of ACTH & Cortisone
418	Davison	Bronchopulmonary Infections in Allergic Individuals
431	Hesser	Facial & Other Head Pain
434	Holinger	Bronchoscopic Technics
436	Hollander	Problems in Use of Cortisone & ACTH
446	Kinney	Hearing Conservation in Children
450	Long	Chemotherapeutic & Antibiotic Agents
456	McNally	Labyrinthine Tests
457	Miller	Laryngeal Emergencies in Infants & Children
460	Myklebust	Deafness in Young Children
466	Richards	Suggestions Concerning Office Practice
471	Sellers	Chronically Infected Ear
472	Seltzer	Plastic Surgery of Nose
479	Spar	Control of Nasal Hemorrhage
485	Teed	Temporal Bone—Horizontal Sections
489	Wilkerson	Hearing & Speech Center for Your City
491	Work	Technic of Endaural Incisions
V	Home Study	Otological Acoustics

SECTION ON INSTRUCTION

ADVANCE ORDER SHEET

All courses cost $1.50 for each period (one hour). Follow instructions explicitly and check for errors in listing before mailing.

Previous to OCTOBER 1

Send order to . . .

WILLIAM L. BENEDICT, M.D., *Executive Secretary-Treasurer*
American Academy of Ophthalmology and Otolaryngology
100 First Avenue Building, Rochester, Minnesota

After OCTOBER 1, mail to . . .

WILLIAM L. BENEDICT, M.D., *Executive Secretary-Treasurer*
American Academy of Ophthalmology and Otolaryngology
c/o Palmer House, Chicago, Illinois

Academy Candidates and Guests May Purchase Tickets at Registration Desk Only

(Over)

ADVANCE ORDER SHEET

ORDERS FILLED ONLY IF CURRENT DUES ARE PAID

NO REFUNDS WILL BE MADE AFTER OCTOBER 12

(Type or Print) Last Name First Name Middle Initial

Office Address

City Zone State

Days to be Present

☐ Monday

☐ Tuesday

☐ Wednesday

☐ Thursday

Total Amount Enclosed $_____

SELECTION OF COURSES ON REVERSE SIDE OF THIS BLANK

RECAPITULATION OF GENERAL INSTRUCTIONS

1. Monday, Tuesday, Wednesday, and Thursday are represented by the letters M, T, W, Th. The first period in the morning is represented by figure 1, second period by figure 2 and third period by figure 3. The first period in the afternoon is represented by figure 4, second period by figure 5, and third period by figure 6. All courses in otolaryngology and maxillofacial surgery are presented in the mornings. All courses in ophthalmology are presented in the afternoons.
2. Reservation of instruction tickets in advance of the meeting will be made ONLY for MEMBERS whose 1951 dues have been paid. Academy candidates and guests may make selection of courses ONLY at the General Registration Desk in Chicago.
3. Make check payable to W. L. Benedict, M.D.
4. Mail order promptly to ensure reservation of first choices. If necessary, an attempt will be made to rearrange schedule to include "first choices."

(Over)

SELECTION OF COURSES

PERIOD		FIRST CHOICE		SECOND CHOICE		THIRD CHOICE	
		Course No.	Lecturer	Course No.	Lecturer	Course No.	Lecturer
MON.	4						
P.M.	5						
	6						
TUES.	1						
A.M.	2						
	3						
P.M.	4						
	5						
	6						
WED.	1						
A.M.	2						
	3						
P.M.	4						
	5						
	6						
THURS.	1						
A.M.	2						
	3						
P.M.	4						
	5						
	6						

News - - - Notes

INTERNATIONAL LEAGUE AGAINST TRACHOMA

The International League Against Trachoma has announced an international prize of one hundred thousand French francs, created by Mrs. Cuenod and Roger Nataf of Tunis, to be awarded in 1952. The prize will be awarded for the best work on etiology, pathogeny, pathologic anatomy or physiology of the trachomatous eye.

Five copies of the work must be sent to the Secretary General of the League Against Trachoma, and it must be accompanied by an abstract of four typed pages (1500 types per page) in French, English, Italian and Spanish. The papers should be submitted to the Secretary General, Dr. Jean Sedan, 94, rue Sylvabelle, Marseilles, before March 1, 1952.

The work receiving the award or its abstracts will be published in the **Revue Internationale du Trachome** in the various languages. The works or abstracts of works not awarded the prize may also be published in extenso or in parts.

The sum of one hundred thousand French francs will be remitted to the prizewinner in the course of the General Meeting in Paris at the time of the Congress of the Societe Francaise d'Ophtalmologie in 1952.

ILLINOIS

The Audiology Foundation will, again this year, offer a limited number of grants-in-aid to students entering into or already engaged in any branch of audiology, including otology, audiometry, speech, acoustics, and education of the deaf or hard of hearing. These grants-in-aid will pay $500.00 per year and will be granted on the recommendation of professional teachers in audiology centers.

For further information in regard to these grants write The Audiology Foundation, 1104 South Wabash Ave., Chicago 5, Ill.

MASSACHUSETTS

At the 170th annual meeting of the Massachusetts Medical Society held on May 22, 1951, Dr. Louisa Paine Tingley, a life member of the Academy, was awarded a "golden anniversary" pin for 50 years membership in the Society.

MISSOURI

An intensive course in pathology of the eye and adnexa will be given by Dr. T. E. Sanders at the Department of Ophthalmology, Washington University School of Medicine, St. Louis, Mo., from Sept. 10 through Sept. 15, 1951. The course will total about 40 hours, including both didactic and microscopic work. Enrollment is limited to 10 students. The tuition fee is $125. Those interested may communicate with the Department of Ophthalmology, Washington University School of Medicine, 640 South Kingshighway Boulevard, St. Louis 10.

NEW YORK

Dr. Arthur J. Bedell, professor emeritus of ophthalmology at Albany Medical College, has just completed a goodwill trip through several Latin American countries. While in Brazil, Dr. Bedell was made an honorary member of the Sao Paulo Ophthalmological Society and foreign corresponding member of the Society of Medicine and Surgery.

PENNSYLVANIA

The Pennsylvania Academy of Ophthalmology and Otolaryngology held its annual meeting May 3-6, 1951, in Wernersville, Pa. The following officers were elected for the coming year: president, Dr. Matthew S. Ersner; president-elect, Dr. Samuel Buckman; vice-presidents, Drs. Chevalier L. Jackson, Paul McCloskey, and Edward H. Campbell; secretary, Dr. Daniel S. DeStio; treasurer, Dr. Bruce A. Grove.

The tenth annual joint meeting of the Reading Dental Society and the Reading Eye, Ear, Nose and Throat Society was held April 18, 1951, at the Abraham Lincoln Hotel. Herbert K. Cooper, D.D.S., director of the Lancaster Cleft Palate Clinic, presented an illustrated talk on the care and treatment of a cleft palate. A study club was conducted on the topic of "Headaches and Head Pain of Rhinologic Origin." Dr. H. Lionel Cunin of Allentown

and Dr. E. A. Palmgren of Lancaster were the instructors.

VIRGINIA

The thirty-second annual meeting of the Virginia Society of Ophthalmology and Otolaryngology was held in Roanoke, May 12, 1951. Dr. Halstead S. Hedges, who has been associated with the University of Virginia since 1890 and is emeritus professor of ophthalmology at the University, was the guest of honor. The lecture in honor of Dr. Hedges was delivered by Dr. Fletcher D. Woodward of Charlottesville. Guest speakers on the program were Dr. John H. Dunnington of New York City and Dr. Louis H. Clerf of Philadelphia.

POSITIONS AVAILABLE

Otolaryngologist: A position for a resident is available at the Episcopal Hospital, Philadelphia, Pa. For details write Dr. Otto C. Hirst, Episcopal Hospital, Philadelphia 25, Pa.

Available: Eye, ear, nose and throat practice grossing approximately $60,000 yearly; own building; available due to death. Terms secondary consideration. For further information write Mrs. W. R. Hickman, 211 Third Street, Logansport, Ind.

The staff of the Lewistown Hospital, Lewistown, Pa., is interested in having a man certified in ophthalmology locate in Lewistown. Lewistown has a population of approximately 16,000 and is located in central Pennsylvania. Lewistown Hospital serves a prosperous agricultural area with a population of approximately 75,000. New construction is under way which will give them a total of 186 beds plus 56 newborn bassinets. The medical staff consists of fourteen active members and thirty-three courtesy members plus two consulting and three honorary members. Write to Mr. Robert A. Kumpf, Administrator, Lewistown Hospital, Lewistown, Pa.

Listings of positions available should be sent to W. L. Benedict, M.D., 100 First Avenue Building, Rochester, Minn., by the fifth of the month preceding publication. They should include (1) type of physician wanted (ophthalmologist or otolaryngologist; diplomate, resident, etc.); (2) type of position to be filled; and (3) whom to write for further information. Unless otherwise requested, listings will be published once only.

The Academy will handle no further correspondence beyond the listing and assume no responsibility. Neither does it endorse or guarantee any of the published listings.

DIRECTORY OF OPHTHALMOLOGIC AND OTOLARYNGOLOGIC SOCIETIES

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 47 Rue de Bellechasse, Paris, France
Secretary-General: Prof. A. Franceschetti, rue A—Jentzer 22, Geneva, Switzerland

International Council of Ophthalmology

President: Prof. F. W. Nordenson
Secretary: Dr. Holger Ehlers, Rigshospital, Copenhagen, Denmark

International Organization Against Trachoma

President: Dr. A. F. MacCallan
Secretary: Dr. F. Wibaut, P. C. Hoofstraat 145, Amsterdam, Holland

Pan-American Association of Ophthalmology

President: Dr. Conrad Berens
Secretary: Dr. Thomas D. Allen, 122 South Michigan Avenue, Chicago 2, Ill.
Time and Place: January 7-12, 1952. Mexico City

Pan-American Association of Ophthalmology, Puerto Rico Chapter

President: Dr. Luis J. Fernandez, Box 2206, San Juan 10, Puerto Rico
Secretary: Dr. P. Fernandez
Place: San Juan

Pan-American Association of Oto-Rhino-Laryngology and Broncho-Esophagology

President: Dr. Jose C. Gros
Time and Place: Third Pan-American Congress of Oto-Rhino-Laryngology and Broncho-Esophagology, Havana, Cuba, Jan. 1952. For information write Dr. Chevalier L. Jackson, 3401 North Broad St., Philadelphia 40, Pa.

Second Latin American Congress of Otorhinolaryngology and Bronchoesophagology

President: Prof. A. dePaula Santos
Secretaries: Dr. Jose deRezende Barbosa and Dr. Plinio de Mattos Barretto, Hospital das Clinicas, Sao Paulo, Brazil
Time and Place: July, 1951, Sao Paulo, Brazil

FOREIGN

All-India Ophthalmological Society

President: Dr. G. Zachariah
Secretaries: Dr. S. N. Cooper and Dr. V. K. Chitnis, Laud Mansion, Queen's Road, Bombay 4, India

Austrian Otolaryngological Society, Vienna

President: Prof. Dr. E. Schlander
Secretary: Doz. Dr. O. Novotny, Vienna IX, Alserstrasse 4, Austria
Time and Place: Annually

Belgian Ophthalmologic Society

President: Dr. L. Weekers
Secretary-General: Dr. M. Appelmans, Avenue Ruelens 179, Louvain
Time and Place: January, June and November. Bruxelles

Bombay Ophthalmologists' Association

Chairman: Rotated
Conveners: Dr. S. N. Cooper and Dr. B. D. Telang, Laud Mansion 21, Queen's Road, Bombay 4
Time and Place: 7:30 p.m., third Wednesday of each month. The seven ophthalmic hospitals of Bombay by rotation

British Association of Otolaryngologists

President: Mr. V. E. Negus
Honorary Secretary: Mr. F. C. W. Capps, 45 Lincoln's Inn Fields, London W. C. 2, England

British Medical Association, Section on Ophthalmology

President: Mr. O. G. Morgan
Secretary: Mr. A. G. Cross, 27 Harley Street, London W. 1, England

Chengtu Ophthalmological Society

President: Dr. Eugene Chan
Secretary: Dr. D. S. Shen, Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China

Chinese Ophthalmology Society

President: Dr. C. H. Chou
Secretary: Dr. F. S. Tsang, 221 Foochow Road, Shanghai

Chinese Ophthalmological Society of Peking

President: Dr. G. C. Lin
Secretary: Dr. H. L. Chen, Ophthalmological Dept., Peking University Medical School, Peking
Time: Bimonthly

Deutsche Ophthalmologische Gesellschaft Heidelberg

President: Prof. Dr. med. K. Wessely
Secretary: Prof. Dr. med. E. Engelking, Heidelberg, Universitäts-Augenklinik

Faculty of Ophthalmologists

President: Dr. Frank W. Law, 45 Lincoln's Inn Fields, London, W.C. 2, England
Secretary: Dr. J. H. Doggart, F.R.C.S.

German Ophthalmological Society

President: Prof. W. Lohlein
Secretary: Prof. E. Engelking, Heidelberg

Hungarian Medical Trade Union, Section of Ophthalmology

President: Prof. I. Csapody
Secretary: Dr. E. Galla, Krisztina Körut 139, Budapest, Hungary
Time and Place: Bimonthly. Second Eye Clinic, Budapest

Hungarian Ophthalmological Society

President: Prof. G. Horay
Assistant Secretary: Dr. Stephen de Grosz, University Eye Hospital, No. 1, Illesucca 15, Budapest

Israel Ophthalmological Society

President: Dr. Aryeh Feigenbaum
Secretary: Dr. E. Sinai, 9 Bialik Street, Tel Aviv

Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

MIDLAND OPHTHALMOLOGICAL SOCIETY
President: Dr. F. A. Anderson
Secretaries: Dr. P. Jameson Evans, 51 Calthorpe Road, Edgbaston, Birmingham 15, England
Dr. R. D. Weeden Butler, 18 Highfield Road, Edgbaston, Birmingham 15, England
Place: Birmingham and Midland Eye Hospital, Church Street, Birmingham 3, England

NEDERLANDSCH OOGHEELKUNDIG GEZELSCHAP
President: Prof. A. W. Mulock Houwer
Secretary: Dr. T. A. Vos, Laan v. Meerdervoort 394, the Hague

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY
President: Mr. A. McKie Reid
Secretary: Mr. W. M. Muirhead, 70 Upper Hanover Street, Sheffield 3, England
Time and Place: October to May. Manchester, Leeds, Newcastle-on-Tyne, Liverpool, Sheffield and Bradford

THE NOVA SCOTIA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. D. M. MacRae
Secretary-Treasurer: Dr. E. I. Glenister, 513 Barrington Street, Halifax, Nova Scotia
Time: Four times yearly at dates to be arranged by the Executive

OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY OF ALBERTA
President: Dr. A. E. Shore
Secretary: Dr. M. R. Marshall, Wells Pavilion, University Hospital, Edmonton, Alberta, Canada
Time and Place: Annual meeting, spring of 1952, Edmonton

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA
President: Dr. Arthur H. Joyce
Secretary: Dr. Arnold L. Lance, 135 Macquarie Street, Sydney, New South Wales

OPHTHALMOLOGICAL SOCIETY OF COPENHAGEN
President: Prof. Dr. Holger Ehlers
Secretary: Dr. Carl Johan Moellenbach, Rigshospitalets oejenafdeling, Copenhagen O, Denmark
Place: Rigshospitalets oejenafdeling

OPHTHALMOLOGICAL SOCIETY OF EGYPT
President: Dr. Ibrahim Ahmad Mohammad
Secretary: Dr. Mahmoud Lutfi, Ophthalmic Hospital, Giza
Time and Place: Annual meeting during March. Summer meeting during August. Dar El Hekmah, 42 Kasr El Ainy Street, Cairo, Egypt

OPHTHALMOLOGICAL SOCIETY OF HOSPITAL DE NUESTRA SENORA DE LA LUZ
Chairman: Dr. Manuel J. Icaza y Dublan
Secretary: Dr. Jorge Meyran, Ezequiel Montes 135, México, D. F.
Time and Place: Second Friday of each month. Hospital de Neustra Senora de la Luz

OPHTHALMOLOGICAL SOCIETY OF NEW ZEALAND
President: Dr. L. S. Talbot
Secretary: Dr. W. J. Hope-Robertson, Kelvin Chambers, 16 The Terrace, Wellington
Time and Place: Annually. Auckland, Wellington, Christchurch and Dunedin alternately

OPHTHALMOLOGICAL SOCIETY OF SOUTH AFRICA
President: Dr. L. Staz
Secretary: Dr. J. Guillaume Louw, 901 Dumbarton House, Adderley Street, Cape Town, South Africa
Time: Annually

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM
President: Mr. M. H. Whiting
Honorary Secretaries: Mr. A. G. Cross and Mr. A. J. B. Goldsmith, 45 Lincoln's Inn Fields, London W. C. 2, England

OPHTHALMOLOGISCHE GESELLSCHAFT IN WIEN
President: K. Lindner
Secretary: Ch. Eyb, Wien, IX, Alserstrasse 4

OXFORD OPHTHALMOLOGICAL CONGRESS
Master: Dr. F. A. Anderson
Hon. Secretary and Treasurer: Ian C. Fraser, F.R.C.S., Red Roofs, Kingsland, Shrewsbury
Time and Place: First week of July 1951, Oxford

PHILIPPINE OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY
President: Dr. Geminiano de Ocampo
Secretary-Treasurer: Dr. Carlos V. Yambao, Philippine General Hospital, Manila

POLISH OPHTHALMOLOGICAL SOCIETY
President: Prof. Dr. W. Kapuscinski
Secretary: Dr. S. Topolski, Piusa 38, Warsaw, Poland
Time and Place: Every two years—summer. Ophthalmic Clinic, Oczki 6, Warsaw

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY
President: Montague Hine, F.R.C.S.
Secretaries: Arthur Lister, F.R.C.S., 56 Wimpole Street, London, W.1., England
H. E. Hobbs, F.R.C.S., 129 Harley Street, London, W.1., England

SAO PAULO SOCIETY OF OPHTHALMOLOGY
President: Dr. Durval Prado
Secretary: Dr. Rubens Belfort Mattos, Rua B. Stapetininga, 29 F-3° andar, Sao Paulo, Brazil

SCOTTISH OPHTHALMOLOGICAL CLUB
President: Dr. E. H. Cameron
Secretary: Dr. John Marshall, 11 Clairmont Gardens, Glasgow, C.3, Scotland
Time and Place: Last Saturday of March and October, Edinburgh and Glasgow, in rotation

SOCIEDAD ARGENTINA DE OFTALMOLOGIA
President: Dr. Diego M. Arguello
Secretary: Dr. Pedro F. Garcia Nocito, Vicente Lopez 1756 A, Buenos Aires, Argentina
Time and Place: Third Wednesday of every month. Buenos Aires

SOCIEDAD CHILENA DE OFTALMOLOGIA
President: Dr. Italo Martini
Secretary: Dr. Adrian Araya Costa, Renaca, no. 34, Santiago, Chile
Place: Santiago

SOCIEDAD COLOMBIANA DE OFTALMOLOGIA Y DE OTORRINOLARINGOLOGIA
President: Dr. Jorge Suarez-Hoyos, Carrera 5a, no. 13-39, Bogota, Colombia
Secretary: Dr. Francisco Arango
Time and Place: Second Tuesday of each month. Club Medico

SOCIEDAD CUBANA DE OFTALMOLOGIA
President: Dr. Oscar F. Horstmann
Secretary: Dr. Heriberto Buch Granados, Calle B No. 668 ent. 27 y 29, Vedado, Habana, Cuba
Time and Place: First Thursday bi-monthly. Malecon No. 61 Bajos, Havana, Cuba

SOCIEDAD MEXICANA DE OFTALMOLOGIA
President: Dr. Teodulo M. Agundis
Secretary: Dr. Jose Luis Arce, Viena 3-5, Mexico D. F., Mexico
Time and Place: 8:30 p.m., first Tuesday of each month, Gral. PRIM 47

SOCIEDAD DE OFTALMOLOGIA DE CORDOBA
Chairman: Dr. Roberto Obregon Oliva
Secretary: Dr. Alberto Urrets Zavalia (hijo), 27 de Abril 255, Cordoba, Argentina

SOCIEDAD DE OFTALMOLOGIA DE GUADALAJARA
President: Dr. Elias Mendoza Gonzalez
Secretary: Dr. Jose Martin del Campo, Av. Juarez 211, Desp. 314, Guadalajara, Jal.
Place: Edificio Lutencia Despacho 101

SOCIEDAD DE OFTALMOLOGIA DEL LITORAL
President: Dr. Juan Manuel Vila Ortiz, Cordoba 1915, Rosario, Argentina
Secretary: Dr. Carlos M. Soto
Time and Place: Last Sunday in every month. Rosario

SOCIEDADE BRASILEIRA DE OFTALMOLOGIA
President: Dr. Natalicio de Farias
Secretary: Dr. Ismar Pereira, Praca Floriano 55, 5° andar, Rio de Janeiro, Brazil
Time: Third Friday of every month from April to December

SOCIEDADE DE OFTALMOLOGIA DEL NORTE
President: Dr. Jorge Luis Castillo
Secretary: Dr. Felix Berman, San Lorenzo 345, Tucuman, Argentina
Place: Mendoza 421, Tucuman

SOCIEDADE DE OFTALMOLOGIA DE MINAS GERAIS
President: Prof. Hilton Rocha
Secretary: Dr. Oswaldo Carvalho
Place: Belo Horizonte, Minas Gerais, Brazil

SOCIEDADE DE OFTALMOLOGIA E OTORINOLARINGOLOGIA DE RIO GRANDE DO SUL
President: Dr. Luiz Assumpcao Osorio
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul

SOCIEDADE DE OTO-RINO-LARINGOLOGIA DO RIO DE JANIERO
President: Dr. Aloysio Novis
Secretaries: Dr. Rubens Cabral, Rua Paissandu 73, Rio de Janeiro, Brazil
Dr. Mairelles Vieira

SOCIEDADE DE OFTALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DE BAHIA
President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil
Secretary: Dr. Adroaldo de Alencar

SOCIETA OFTALMOLOGICA ITALIANA
President: Prof. Giuseppe Ovio
Secretary: Prof. E. Leonardi, Piazza degli Eroi, 11 Roma, Italy
Place: Roma Piazza degli Eroi 11

SOCIETE BELGE D'OPHTALMOLOGIE
President: Dr. L. Weekers
Secretary-General: Dr. M. Appelmans, 179 avenue Reulens, Louvain, Belgium
Time: Last Sunday of February, June and November

SOCIETE FRANCAISE D'OPHTALMOLOGIE
Administrateur: G. Raimond, 17et19, Rue de Buci, Paris (VI«) France

SOCIETY OF SWEDISH OPHTHALMOLOGISTS
President: Prof. S. Larsson
Secretary: Dr. K. O. Granstrom, Sodermalmstorg 4, Stockholm, Sweden

SOUTHERN OPHTHALMOLOGICAL SOCIETY, ENGLAND
President: Campbell Shaw, M. R. C. S.
Hon. Secretary and Treasurer: Nigel Cridland, D.M., D.O., 25 Craneswater Park, Southsea, England
Time and Place: Sept. 29, 1951, Salisbury General Hospital, Salisbury; Oct. 27, 1951, Portsmouth and Southern Counties Eye and Ear Hospital, Southsea

NATIONAL

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Derrick Vail
Executive Secretary-Treasurer: Dr. William L. Benedict, 100 First Avenue Building, Rochester, Minn.
Time and Place: October 14-19, 1951, Chicago

AMERICAN ASSOCIATION OF EYE, EAR, NOSE AND THROAT SOCIETY SECRETARIES
President: Dr. Kenneth L. Craft
Secretary-Treasurer: Dr. Daniel S. DeStio, Highland Building, Pittsburgh 6, Pa.

AMERICAN LARYNGOLOGICAL ASSOCIATION
President: Dr. Gordon B. New
Secretary: Dr. Louis H. Clerf, 1530 Locust, Philadelphia 2, Pa.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, INC.
President: Dr. Louis H. Clerf
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Building, Rochester 7, N. Y.
EASTERN SECTION
Vice-President: Dr. Harry P. Schenck
Secretary: Dr. Francis W. Davison, Geisinger Memorial Hospital, Danville, Pa.
MIDDLE SECTION
Vice-President: Dr. Clarence W. Engler
Secretary: Dr. Walter H. Theobald, 307 North Michigan Avenue, Chicago 1, Ill.

SOUTHERN SECTION:
Vice-President: Dr. Charles C. Grace
Secretary: Dr. James W. McLaurin, Raymond Building, Baton Rouge 6, La.

WESTERN SECTION:
Vice-President: Dr. Lewis F. Morrison
Secretary: Dr. Harold Boyd, 1136 West Sixth Street, Los Angeles, Calif.

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY
Chairman: Dr. A. Ray Irvine
Secretary: Dr. Trygve Gundersen, 101 Bay State Road, Boston, Mass.

AMERICAN MEDICAL ASSOCIATION, SECTION ON LARYNGOLOGY, OTOLOGY AND RHINOLOGY
Chairman: Dr. James M. Robb
Secretary: Dr. Sam H. Sanders, 1089 Madison Avenue, Memphis 3, Tenn.

AMERICAN OPHTHALMOLOGICAL SOCIETY
President: Dr. John H. Dunnington
Secretary-Treasurer: Dr. Maynard C. Wheeler, 30 West 59th Street, New York 19, N. Y.

AMERICAN OTOLOGICAL SOCIETY
President: Dr. Kenneth Day
Secretary: Dr. John R. Lindsay, 950 East 59th Street, Chicago 37, Ill.

AMERICAN OTORHINOLOGIC SOCIETY FOR THE ADVANCEMENT OF PLASTIC AND RECONSTRUCTIVE SURGERY
President: Dr. Norman N. Smith
Secretary: Dr. Joseph G. Gilbert, 111 East 61st Street, New York 21, N. Y.

AMERICAN SOCIETY OF OPHTHALMOLOGIC AND OTOLARYNGOLOGIC ALLERGY
President: Dr. William H. Evans
Secretary-Treasurer: Dr. Joseph W. Hampsey, 806 May Building, Pittsburgh 22, Pa.
Time and Place: Annual meeting, October 19, 1951, Chicago.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.
Chairman: Dr. Walter H. Fink
Secretary-Treasurer: Dr. James H. Allen, 1430 Tulane Avenue, New Orleans, La.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY
President: Dr. R. G. C. Kelly
Secretary: Dr. J. Clement McCulloch, 380 Medical Arts Building, Toronto, Ontario

CANADIAN OPHTHALMOLOGICAL SOCIETY
President: Dr. R. F. Nicholls
Secretary: Dr. J. F. A. Johnston, 174 St. George Street, Toronto, Ontario

CANADIAN OTOLARYNGOLOGICAL SOCIETY
President: Dr. W. J. McNally
Secretary: Dr. Jules Brahy, 361 Sherbrooke Street East, Montreal 18, Quebec

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS, INC.
President: Mr. Mason H. Bigelow
Secretary: Dr. Franklin M. Foote, 1790 Broadway, New York 19, N. Y.

REGIONAL

ARK-LA-TEX OTO-OPHTHALMIC SOCIETY
President: R. R. Kirkpatrick
Secretary: Dr. Frank L. Bryant, 2622 Greenwood, Shreveport, La.
Time and Place: First Monday of month, September through June. Shreveport Club

HAWAII EYE, EAR, NOSE AND THROAT SOCIETY
Chairman: Dr. Ogden D. Pinkerton
Secretary: Dr. John P. Frazer, 1133 Punchbown Street, Honolulu, T. H.
Time and Place: Third Thursday of each month (dinner meetings). Pacific Club, Honolulu

INTER-MOUNTAIN OTO-OPHTHALMOLOGICAL SOCIETY
President: Dr. Homer E. Smith
Secretary: Dr. George R. Ely, 115 East South Temple Street, Salt Lake City, Utah
Time and Place: Third Monday of each month, September through May. University Club, 136 East South Temple, Salt Lake City

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY
President: Dr. S. B. Carruthers
Secretary: Dr. Edley H. Jones, 1301 Washington Street, Vicksburg, Miss.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY
President: Dr. Benjamin A. Sachs
Secretary: Dr. Garrett L. Sullivan, 101 Bay State Road, Boston 15, Mass.
Time and Place: Third Wednesday of each month, November through April. Massachusetts Eye and Ear Infirmary

NEW ENGLAND OTO-LARYNGOLOGICAL SOCIETY
President: Dr. Robert L. Goodale
Secretary-Treasurer: Dr. Burton E. Lovesey, 76 Bay State Road, Boston 15, Mass.
Time and Place: Quarterly. Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY
President: Dr. Augustus B. Dykman
Secretary-Treasurer: Dr. Howard P. House, 1136 West Sixth Street, Los Angeles 14, Calif.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. William B. Hubbard
Secretary: Dr. Frank A. Ware, 514 Genesee Bank Bldg., Flint, Mich.
Time and Place: Second Tuesday evening of each month, except summer months. Bancroft Hotel, Saginaw

SIOUX VALLEY EYE AND EAR ACADEMY
President: Dr. James Reeder, Jr.
Secretary-Treasurer: Dr. W. P. Davey, 627-632 Frances Building, Sioux City, Iowa

SOUTHERN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY
Chairman: Dr. Francis E. Le Jeune
Secretary: Dr. Edley H. Jones, 1301 Washington Street, Vicksburg, Miss.

WISCONSIN-UPPER MICHIGAN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. James K. Trumbo
Secretary: Dr. G. L. McCormick, 650 South Central Avenue, Marshfield, Wis.
Time and Place: May 1951. Wausau, Wis.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION
President: Dr. C. G. Hinkle
Secretary: Dr. K. W. Cosgrove, 113 East Capitol Avenue, Little Rock, Ark.

CALIFORNIA MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION
Chairman: Dr. George F. Keiper, Jr.
Secretary: Dr. Maurice W. Nugent, 2007 Wilshire Blvd., Los Angeles 5, Calif.

COLORADO OPHTHALMOLOGICAL SOCIETY
President: Dr. J. Leonard Swigert
Secretary: Dr. James C. Strong, 227 Sixteenth Street, Denver, Colo.
Time and Place: Every third Saturday. Colorado Medical Center

COLORADO OTOLARYNGOLOGICAL SOCIETY
President: Dr. Edgar A. Elliff
Secretary: Dr. James Chessen, 510 Republic Building, Denver 2, Colo.
Time and Place: First Saturday of each month, October through May. Colorado University School of Medicine

FLORIDA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. W. Jerome Knauer
Secretary-Treasurer: Dr. Charles C. Grace, 145 King Street, St. Augustine, Fla.

GEORGIA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Lester A. Brown
Secretary: Dr. Braswell E. Collins, 701 Elizabeth Street, Waycross, Ga.
Time and Place: First Friday and Saturday of March General Oglethorpe Hotel, Savannah, Ga.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. E. W. Dyar
Secretary-Treasurer: Dr. M. S. Harding, 308 Hume Mansur Building, Indianapolis, Ind.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. George Albright
Secretary: Dr. Carl A. Noe, 601-611 Highley Building, Cedar Rapids, Iowa
Time and Place: 1951—Iowa City

KANSAS STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. N. L. Francis
Secretary: Dr. W. D. Pitman, First National Bank Building, Pratt, Kan.

MASSACHUSETTS MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY
Chairman: Dr. James J. Regan
Secretary: Dr. Lawrence R. Dame, 78 Federal Street, Greenfield, Mass.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY
Chairman: Dr. J. E. Croushore (Otolaryngology)
Co-Chairman: Dr. J. C. Gemeroy (Ophthalmology)
Secretary: Dr. R. W. Teed, 215 South Main, Ann Arbor, Mich. (Otolaryngology)
Co-Secretary: Dr. F. B. Heckert, 1105 Bank of Lansing Building, Lansing, Mich. (Ophthalmology)

MICHIGAN TRIOLOGICAL SOCIETY
President: Dr. William D. Irwin
Secretary: Dr. V. E. Cortopassi, 324 South Washington Avenue, Saginaw, Mich.
Time: Second Thursday of November, December, March, April and May

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Malcolm C. Pfunder
Secretary-Treasurer: Dr. Frank Adair, 822 Lowry Medical Arts Building, St. Paul 2, Minn.
Time and Place: Second Friday of each month, November through May. Alternating, Minnesota Club, St. Paul, and Minneapolis Club, Minneapolis

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY
President: Dr. W. L. Forster
Secretary-Treasurer: Dr. F. D. Hurd, Medical Arts Building, Great Falls, Mont.
Time and Place: Semi-annually. Summer, Bozeman; mid-winter, Diamond S Ranchotel, Boulder

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY
President: Dr. G. M. Billings
Secretary: Dr. MacLean B. Leath, 529 North Main Street, High Point, N. C.
Time and Place: Annually, beginning second Monday in September.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Richard S. Fixott
Secretary: Dr. George E. Chamberlain, 909 Medical Dental Building, Portland 5, Ore.
Time and Place: Third Tuesday each month September through May. Old Heathman Hotel, Portland

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Matthew S. Ersner
Secretary: Dr. Daniel S. DeStio, Highland Building, Pittsburgh 6, Pa.

PUERTO RICO MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Luis J. Fernandez
Secretaries: Dr. Ricardo F. Fernandez, P.O. Box 2206, San Juan 10, Puerto Rico (Ophthalmology)
Dr. Carlos E. Munoz MacCormick, P.O. Box 604, San Juan, Puerto Rico (Otolaryngology)
Time and Place: Bimonthly. Puerto Rico Medical Association Building

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. William M. Carpenter
Secretary-Treasurer: Dr. Roderick Macdonald, Rock Hill, S. C.

TENNESSEE STATE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Sam H. Sanders
Secretary-Treasurer: Dr. Roland H. Myers, 1720 Exchange Building, Memphis, Tenn.
Time: Annually

TEXAS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. V. R. Hurst
Secretary: Dr. John L. Matthews, 414 Navarro Street, San Antonio 5, Texas

VIRGINIA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Robert H. Courtney
Secretary-Treasurer: Dr. G. Slaughter Fitz-Hugh, 104 East Market St., Charlottesville, Va.
Time: May 1952

WEST VIRGINIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Garnett P. Morison
Secretary: Dr. Melvin W. McGehee, 425 Eleventh Street, Huntington 1, W. Va.
Time: Biannual

LOCAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT
Chairman: Dr. William F. Krone
Secretary: Dr. Francis J. Grant, 1224 Salem Avenue, Hillside, N. J.
Time and Place: 8:45 p.m., second Monday of the month. The Academy of Medicine, 91 Lincoln Park, South, Newark

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. C. R. Anderson
Secretary-Treasurer: Dr. A. L. Peter, 406 Akron Savings and Loan Building, Akron, Ohio
Time and Place: 6:30 p.m., first Monday in Januarv March, May and November. Akron City Club

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY
President: Dr. Edward S. Wright
Secretary-Treasurer: Dr. James T. King, 384 Peachtree Street N.E., Atlanta 3, Ga.
Time and Place: 7:30 p.m., fourth Monday of each month, October to May. Academy of Medicine

BALTIMORE CITY MEDICAL SOCIETY, OPHTHALMOLOGICAL SECTION
Chairman: Dr. M. Elliott Randolph
Secretary-Treasurer: Dr. Abraham Kremen, 2355 Eutaw Place, Baltimore 17, Md.
Time and Place: 8:00 p.m., fourth Thursday of every month October to May. Medical and Chirurgical Faculty, 1211 Cathedral St.

BIRMINGHAM EYE, EAR, NOSE AND THROAT SOCIETY
President: Each member, in alphabetical order.
Secretary: Dr. David A. McCoy, Woodward Building, Birmingham, Ala.
Time and Place: 6:30 p.m., second Tuesday of each month, September through May. Thomas Jefferson Hotel

BOSTON CITY HOSPITAL AURAL AND OPHTHALMIC ASSOCIATION
President: Dr. Joseph Nerbonne
Secretary: Dr. Benjamin Riseman, 41 Bay State Road, Boston 15, Mass.

BROOKLYN OPHTHALMOLOGICAL SOCIETY
President: Dr. Mortimer A. Lasky
Secretary-Treasurer: Dr. Louis Freimark, 256 Rochester Avenue, Brooklyn 13, N. Y.
Time and Place: 8 p.m., third Thursday in October, December, February and April. Medical Society of the County of Kings, 1313 Bedford Avenue

BUFFALO OPHTHALMOLOGIC CLUB
President: Dr. Arthur L. Bennett
Secretary: Dr. Herbert R. Reitz, 446 Linwood Avenue, Buffalo, N. Y.
Time and Place: Second Thursday of each month, October through May. Park Lane

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Harold R. Watkins
Secretary-Treasurer: Dr. Philip R. McGrath, 843 Jefferson Building, Peoria, Ill.

CENTRAL NEW YORK EYE, EAR, NOSE AND THROAT SOCIETY
President: Dr. Cecil B. Hert
Secretary-Treasurer: Dr. James L. McGraw, 619 University Building, Syracuse, N. Y.

CHATTANOOGA EYE, EAR, NOSE AND THROAT SOCIETY
Chairman and Secretary: Dr. Willard H. Steele, Jr., 552 McCallie Avenue, Chattanooga, Tenn.
Time and Place: 6:30 p.m., fourth Thursday in each month, October through May. Mountain City Club

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY
President: Dr. Oliver E. Van Alyea
Secretary: Dr. Lawrence J. Lawson, 636 Church Street, Evanston, Ill.

CHICAGO OPHTHALMOLOGICAL SOCIETY
President: Dr. J. Robert Fitzgerald
Secretary-Treasurer: Dr. Gail E. Soper, 636 Church Street, Evanston, Ill.
Time and Place: 7:30 p.m., third Monday of each month, October to May. Chicago-Illini Union, 715 S. Wood Street

CINCINNATI OPHTHALMOLOGIC CLUB
Presidium: Dr. Donald J. Lyle, Dr. Karl W. Ascher, Dr. Josef D. Weintraub
Secretary: Dr. Josef D. Weintraub, 715 Provident Bank Building, Seventh and Vine Streets, Cincinnati, Ohio
Time and Place: Second Wednesday night of month, November through May. University Club, Fourth and Broadway

CLEVELAND OPHTHALMOLOGICAL CLUB
President: Dr. G. Leslie Miller
Secretary-Treasurer: Dr. Webb P. Chamberlain, Jr., 7405 Detroit Avenue, Cleveland, Ohio
Time and Place: Second Tuesday of November, January, February and April. Statler Hotel, Cleveland

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY
Chairman: Dr. Wilfred E. Fry
Clerk: Dr. M. Luther Kauffman, Medical Arts Building, Jenkintown, Pa.
Time and Place: 8:15 p.m., third Thursday of every month, October through April. College of Physicians Building

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY
President: Dr. Rex E. House
Secretary-Treasurer: Dr. L. David Wright, Thomas-Spann Clinic, 1546 South Brownlee, Corpus Christi, Texas
Time and Place: First Wednesday of each month. La Louisiane

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. W. B. Wilkinson
Secretary: Dr. Claude D. Winborn, Medical Arts Building, Dallas 1, Texas
Time and Place: First Tuesday of each month. Melrose Hotel

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. J. H. McNamee
Secretary-Treasurer: Dr. H. H. Gurau, 213 Bankers Trust Building, Des Moines, Iowa
Time and Place: 6:00 p.m., fourth Monday of each month, September through May. Des Moines Club

DETROIT OPHTHALMOLOGICAL CLUB
Secretary-Treasurer: Dr. Frederick A. Lauppe, 1249 David Whitney Building, Detroit 26, Mich.

DETROIT OPHTHALMOLOGICAL SOCIETY
President: Dr. Cecil Lepard
Secretary: Dr. Arthur P. Wilkinson, 947 Fisher Building, Detroit 2, Mich.
Time and Place: Second Monday of each month, November through April. Wayne County Medical Society

DETROIT OTO-LARYNGOLOGICAL SOCIETY
President: Dr. B. F. Glowacki
Secretary-Treasurer: Dr. John R. Birch, 1010 Maccabees Building, Detroit 2, Mich.
Time and Place: Third Wednesday of each month, September to May. Wayne County Medical Society Building

EAR, NOSE AND THROAT CLUB OF ST. LOUIS
Chairman: Dr. Bernard J. McMahon
Secretary: Dr. Harry N. Glick, 1504 Grand Boulevard, St. Louis, Mo.
Time and Place: Third Wednesday in November, January, March and May. University Club Bldg.

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION
President: Dr. Byron H. Porter
Secretary-Treasurer: Dr. E. Martin Freund, 762 Madison Avenue, Albany 3, N. Y.
Time and Place: 8 p.m., first Thursday of month, October to June. Albany, Troy, Schenectady, rotating monthly

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY
President: Dr. W. H. McKenzie
Secretary: Dr. C. Keith Barnes, 921 Neil P. Anderson Building, Fort Worth 2, Texas
Time and Place: 6:30 p.m., first Friday of each month, except July and August. All Saints' Hospital

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SECTION
President: Dr. Lyle Hooker
Secretary: Dr. Claude C. Cody, III, 1304 Walker Avenue, Houston 2, Texas
Time: Second Thursday of each month, October through June

INDIANAPOLIS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY
President: Dr. Edwin D. Dyar
Secretary-Treasurer: Dr. J. Lawrence Sims, 809 Hume Mansur Building, Indianapolis 4, Ind.
Time and Place: 6:30 p.m., second Thursday of each month, November to May. Indianapolis Athletic Club

KANSAS CITY SOCIETY OF O. O. R. L.
President: Dr. John S. Knight
Secretary: Dr. Barnard C. Trowbridge, 411 Alameda Road, Kansas City 2, Mo.
Time and Place: Third Thursday of the month, November through May. Hotel President, 14th and Baltimore

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY
President: Dr. Edmund D. Godwin
Secretary: Dr. James V. Keipp, 110 Pine Avenue, Long Beach 2, Calif.
Time and Place: 6:00 p.m., monthly, September through May. Seaside Memorial Hospital

LOS ANGELES OPHTHALMOLOGICAL SOCIETY
President: Dr. Deane C. Hartman
Secretary: Dr. Daniel B. Esterly, 104 North Madison Avenue, Pasadena 1, Calif.
Time and Place: First Thursday of each month, September through June. Los Angeles County Medical Society Building, 1925 Wilshire Boulevard

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. Alden H. Miller
Secretary: Dr. Victor Goodhill, 2007 Wilshire Boulevard, Los Angeles 5, Calif.
Time and Place: 6:00 p.m., fourth Monday of each month, September through May. Los Angeles County Medical Association Building, 1925 Wilshire Boulevard

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION ON OTOLARYNGOLOGY
President: Dr. Victor Alfaro
Secretary: Dr. Frasier Williams, 1228 North Irving Street, Arlington, Va.
Time and Place: 7:00 p.m., third Tuesday in October, November, March and May. Army and Navy Club, 17th and Farragut Square, N.W.

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
Chairman: Each member, in alphabetical order
Secretary: Dr. Sam H. Sanders, 1089 Madison Avenue, Memphis, Tenn.
Time and Place: Second Tuesday in each month, September through May. Memphis Eye, Ear, Nose and Throat Hospital

MILWAUKEE OTO-OPHTHALMIC SOCIETY
President: Dr. J. P. Wild
Secretary-Treasurer: Dr. Howard High, 324 East Wisconsin Avenue, Milwaukee 2, Wis.
Time and Place: 6:30 p.m., fourth Tuesday of each month, October to May. Athletic Club

MONTGOMERY COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT
President: Dr. Robert A. Bruce
Secretary-Treasurer: Dr. L. N. Shroder, 144 West Fourth Street, Greenville, Ohio
Time and Place: First Tuesday of November, February, March and May. Dayton Country Club

MONTREAL OPHTHALMOLOGICAL SOCIETY
President: Dr. Jules Brahy
Secretary-Treasurer: Dr. Leo S. S. Kirschberg, 1390 Sherbrooke Street West, Montreal, Que., Canada
Time: Second Thursday of October, December, February and April

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. N. B. Morris
Secretary-Treasurer: Dr. Herbert Duncan, Bennie Dillon Building, Nashville, Tenn.
Time and Place: Third Monday evening of month, October through May. James Robertson Hotel

NEW YORK ACADEMY OF MEDICINE, SECTION ON OPHTHALMOLOGY
Chairman: Dr. James W. Smith
Secretary: Dr. A. Gerard De Voe, 30 West 59th St., New York, N. Y.
Time and Place: Third Monday of the month, October through May. New York Academy of Medicine

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY
President: Dr. Samuel Gartner
Secretary: Dr. Leon H. Ehrlich, 211 Central Park West, New York 24, N. Y.
Time and Place: First Monday of the month, October to May. New York Academy of Medicine

NUECES COUNTY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. N. Meador
Secretary: Dr. Rex C. House, 228 Medical-Dental Building, Corpus Christi, Texas
Time and Place: 7:30 p.m., second Monday of each month, October through May. Dusty's, 1739 South Brownlee Street, Corpus Christi, Texas

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. C. W. McClure
Secretary: Dr. Richard A. Clay, 416 Northwest 13th Street, Oklahoma City, Okla.
Time and Place: First Tuesday of each month. University Hospital, 800 Northeast 13th Street, Oklahoma City

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Thomas T. Smith
Secretary-Treasurer: Dr. G. T. Alliband, 1020 Medical Arts Building, Omaha, Neb.
Time and Place: Dinner meeting third Wednesday monthly, October to May. Omaha Club

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

Chairman: Dr. Alfred Cowan
Secretary: Dr. John W. Deichler, 301 South 21st Street, Philadelphia 3, Pa.
Time: First Thursday of each month, November through April

PHILADELPHIA LARYNGOLOGICAL SOCIETY

President: Dr. Thomas F. Furlong, Jr.
Secretary: Dr. John J. O'Keefe, 255 South 17th Street, Philadelphia 3, Pa.

PITTSBURGH ACADEMY OF MEDICINE

President: Dr. John S. Plumer
Secretary: Dr. Samuel D. Evans, 1501-2 Park Building, Pittsburgh 22, Pa.
Time and Place: 8:00 p.m., fourth Monday of each month, October through May. Pittsburgh Academy, 322 North Craig Street

PITTSBURGH OTOLOGICAL SOCIETY

President: Dr. Daniel S. DeStio
Secretary: Dr. George C. Schein, 634 Washington Road, Pittsburgh, Pa.
Time and Place: Bimonthly

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. John F. Tolan
Secretary-Treasurer: Dr. Willard F. Goff, 432 Stimson Building, 1215 Fourth Avenue, Seattle 1, Wash.
Time and Place: Third Tuesday of each month. Medical-Dental Building, Seattle

READING EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Roy Deck
Secretary: Dr. Benjamin F. Souders, 143 North Sixth Street, Reading, Pa.
Time and Place: Third Wednesday of each month, September to July (dinner meetings). Wyomissing Club

RICHMOND, VIRGINIA, EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Edwin D. Vaughan
Secretary-Treasurer: Dr. Charles N. Romaine, 1001 West Franklin Street, Richmond 20, Va.
Time and Place: First Tuesday of January, March, May and October. Commonwealth Club

ST. LOUIS COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Anderson C. Hilding
Secretary: Dr. James P. Tetlie, 626 Medical Arts Building, Duluth, Minn.
Time and Place: 6:00 to 8:00 p.m., preceding the monthly St. Louis County Medical Society meeting St. Mary's Hospital, Duluth

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. J. M. Keller
Secretary: Dr. Benjamin Milder, 539 North Grand Avenue, St. Louis 3, Mo.
Time and Place: 8:00 p.m., fourth Friday of each month, October through April, except December. Elliott Auditorium, McMillan Hospital

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. W. E. Borley, 655 Sutter Street, San Francisco, Calif.
Secretary: None
Time and Place: Fourth Tuesday of each month, except July, August and December. San Francisco County Medical Society Building

SECTION ON OPHTHALMOLOGY OF THE MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA

President: Dr. Everett S. Caldemeyer
Secretary-Treasurer: Dr. J. Spencer Dryden, 1835 Eye Street Northwest, Washington 6, D. C.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Phil Greene
Secretary: Dr. Cornelius E. Hagan, Jr., 508 Old National Bank Building, Spokane, Wash.
Time and Place: Fourth Tuesday of each month, September through May. Paulsen Medical and Dental Building

SUPERIOR CALIFORNIA EYE CLUB

President: Dr. Theodore Holstein, 523 Medico-Dental Building, Sacramento 14, Calif.
Secretary: Dr. John Berg
Time: Every third Thursday, eight months of the year

TOLEDO EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. N. Gardner Mathieson
Secretary: Dr. Robert D. Kiess, 1838 Parkwood, Toledo, Ohio
Time and Place: Third Tuesday of each month, November through May, Toledo Club

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. Joseph C. Hill
Secretary: Dr. Harold R. Sniderman, 220 Bloor Street West, Toronto 5, Ontario, Canada
Time and Place: Second Monday night of November, January, February and March. Academy of Medicine, Toronto

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. E. Imbrie
Secretary-Treasurer: Dr. F. E. Murdock, 28½ West Scribner Avenue, DuBois, Pa.
Time: Biannually. Third Thursdays of May and October

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

President: Dr. Vincent Gallizzi
Secretary: Dr. Samuel T. Buckman, 70 South Franklin Street, Wilkes-Barre, Pa.
Time and Place: Last Tuesday of each month, October through May, except December. Luzerne County Medical Society Library, 130 South Franklin Street

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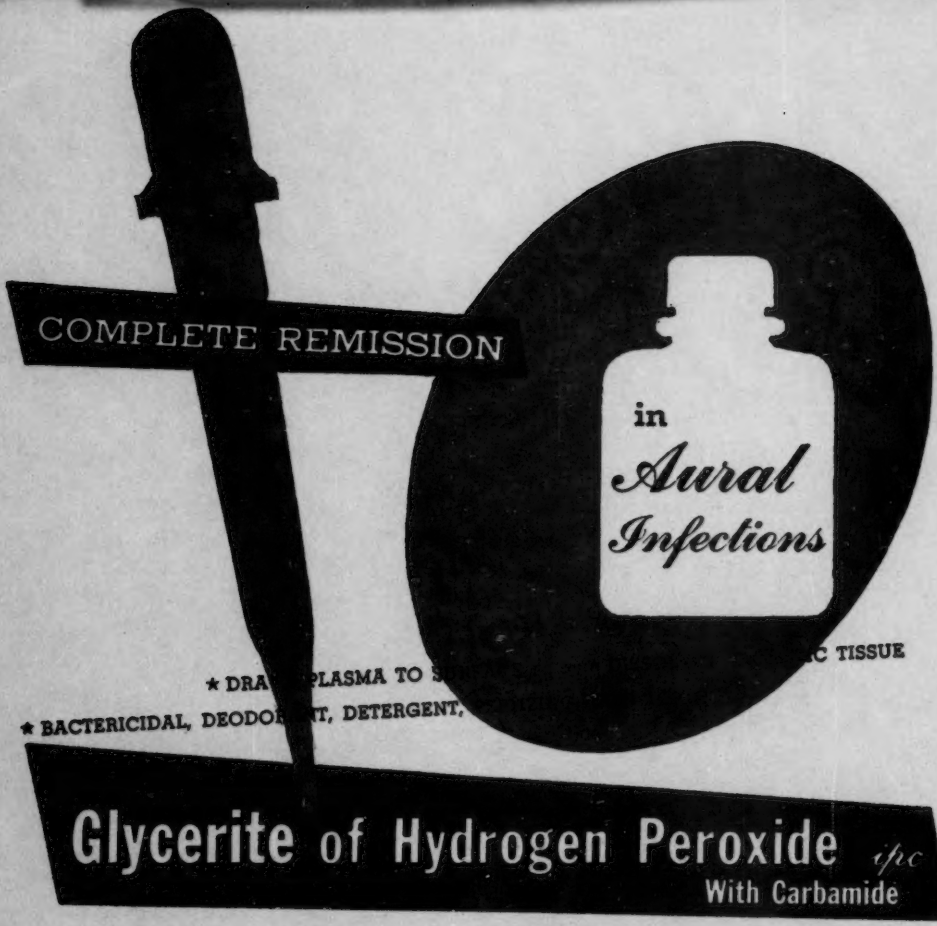

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E., E., N., & T. Mo., 26:27, 1947.
Laryngoscope, 56:556, 1946.
New Eng. J. Med., 234:468, 1946.
Annals of Allergy, 4:33, 1946.
J. A. Ph., A., (Sc. Ed.) 35:304, 1946.

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